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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 12 1952

British Medical Association

ONE HUNDRED AND TWENTIETH ANNUAL MEETING, DUBLIN, 1952

President's Address

TOPICS, THOUGHTS, AND TENDENCIES

BY

P. T. O'FARRELL, M.D., F.R.C.P.I., D.P.H., D.T.M.
Senior Physician, St. Vincent's Hospital, Dublin

When you did me the signal honour of appointing me President-Elect of the British Medical Association I took courage from some lines of the oft-quoted sentence, "Be not afraid of greatness . . . some have greatness thrust upon them." It is in this spirit that I now address you as President, first thanking you, my friends, for the distinction you have conferred on me. In doing honour to me you have bestowed an even greater honour on my Irish colleagues, and on their behalf I extend to you their most grateful thanks.

The office of President of the B.M.A. in the past has been filled by so many distinguished men that I hesitate to select any particular name for mention. But it would be discourteous if I did not refer to one who, by his dignity and erudition, has served you so well. I refer, of course, to our friend Sir Henry Cohen. Your immediate Past-President, Dr. Sichel, has also played a leading part in looking after your interests from far distant lands. No President of the British Medical Association could venture to undertake the responsibilities of his high office without the full support and approbation of his fellow members. It is on these considerations that I ask you to give me your full-hearted co-operation, for I am anxious to be in harmony with your wishes.

In the past the B.M.A. has met in Ireland on no fewer than six occasions. By reference to back copies of the *Journal* one can infer that the meetings in Dublin, Belfast, and Cork were highly successful, and that infiltration of the B.M.A. by Irish blood has not given rise to any incompatibility. We now meet in Dublin for the fourth time, previous meetings having been held in the years 1867, 1887, and 1933, with William Stokes, John Banks, and T. G. Moorhead as Presidents.

The achievements of these great men are well known. The two who have passed beyond our ken have left their names inscribed in the annals of medicine. Happily, Moorhead is still with us. This occasion should not be let pass without paying a special tribute to him. He has brushed aside adversity with a courage and a fortitude that have never faltered. We admire him for his wisdom, knowledge, and high ideals. He is truly an ornament to the profession, a gentleman indeed in whom we place an infinite trust.

It is interesting to recall, in a rapid survey, some of the events of previous annual meetings in Dublin, and to try to contrast them with our present conjoint meeting. At all meetings there has been a unity of purpose to bring the profession together socially and academically, and to explore the ramifications of medical politics in relation to the times.

In these days of austerity it might perhaps be as well to gloss over the social amenities of the past, for they were intimately connected with the value of currency and a more leisurely way of life. Some of us will no doubt miss the excursions by the four-in-hand coaches, Tantivy and Hirondelle, which were special features of the meeting of 1887. Nevertheless, enjoyment is a matter for the present, for in the retrospect only the pleasant memories remain.

Contributions to Medical Science

On the academic side it is on record that scientific sessions of the B.M.A. were inaugurated for the first time at the Dublin Meeting of 1867. Of world-wide importance was the address by Joseph Lister "On the Antiseptic Principle of the Practice of Surgery." We in Dublin are proud that from this city came forth the first public pronouncement on the antiseptic principle.

At other annual meetings in Dublin many important contributions to medicine were made; but they are too numerous to mention now. One can, however, hardly pass over the contributions of Kocher, of Berne, and of Unna, of Hamburg, to the B.M.A. meeting of 1887. Some of us will remember the important paper by Dr. Winnett Orr, on the treatment of chronic osteomyelitis at the meeting of 1933.

In connexion with our present meeting Plenary Scientific Sessions are being started for the first time. Another new development is the holding of a Scientific Exhibition. Both these innovations are well worthy of support, for they foreshadow even greater things to come. The Hobbies Exhibition in Dublin in 1933 is being revived again this year, probably because we think, like some Americans, that "a hobby is something you go goofy over to keep from going nuts over things in general."

Nowadays medical politics occupy a much more prominent place in the Association's activities than heretofore, so later on some reference will have to be made to the subject. Since the foundation of the B.M.A. there has always been close and harmonious co-operation between members of the medical profession on either side of the Irish Sea. A kind of professional parallelism existed, and still exists, although these lines of symmetry have sometimes wavered under the impact of political evolution and legislative enactments.

Bonds of Friendship

These evolutionary changes have not in any way altered the good relations between the B.M.A. and the I.M.A.—in fact, the bonds of friendship have become more closely knit. In evidence thereof the B.M.A. has recently afforded generous financial facilities to the I.M.A. for the purchase of new premises, and the holding of a joint meeting this year shows a spirit of co-operation and good will which augurs well for the future. To assure continuation of these good relations some attention must be paid to the different problems which the two Associations have to face. Owing to legislative enactments, both old and new, the pattern of medical practice has been and is likely to be dissimilar in both countries. But where there may be variations in methods of practice there should be uniformity in matters of precept.

The B.M.A. is obviously dissatisfied with some of the provisions of the National Health Service and has voiced the hope that reforms will be made under amending legislation. The recent Danckwerts Award, while meeting the just claim of the doctors on a financial issue, does not of course remedy many other grievances connected with the working of the National Health Service. While the I.M.A. is not likely to be faced by a National Health Service on the British lines, it does fear the imposition of bureaucratic State control, which it will strenuously oppose. It is unnecessary to burden you with the reasons for this opposition; it is not in the nature of a maverick revolt, nor is it based on the whimsy notion of being "agin the Government." There is no doubt, however, that undue intrusion of the State into the practice of medicine is a matter of grave concern to both Associations.

Upholding of Principles

The high ethical standards of our profession must not be allowed to waver at the behest of those who would lower our dignity and cause us to forfeit our allegiance to our high tradition. We as a profession occupy a privileged position in society which can be maintained only by strictly upholding the principles on which the privilege was granted.

In recent years the concept of the Welfare State has been gaining considerable public support, particularly as one of its main ideals is to entrust the State with responsibility for the health of the people. This doctrine is, of course, not entirely unobjectionable—in fact, the whole of modern State medicine comes within its tenets. But the doctrine would be repugnant if it were to envisage an exclusive or excessive responsibility of the State over the liberty of the individual and the family way of life. This danger is not yet fully realized by the public, for they may be misled by political clamour and subtle propaganda into thinking that State monopoly over the health of the people would be a Utopian achievement.

Exclusive or excessive State responsibility would mean large-scale State control and administration by Government fiat. Under such a system the medical profession would lose its independence; the impulse for individual incentive would be blunted, and the public would suffer as a consequence. As a warning of these dangers attention should be paid to the dictum of Cervantes that "everyone is the artificer of his own misfortune." One freely admits that social medicine has conferred estimable benefits on the community and that still more can be done to extend the scope of its activities. In this crusade the medical profession should take a leading part in its endeavour that the best of medicine should be made available for all. To achieve success there should be harmonious and continuous partnership between Governments, the medical and allied professions, and responsible leaders of the community.

The recent expansion of social medicine and of national health services has led to a new relationship between the doctor and State in which the position of the general practitioner seems to have been adversely affected. It is common belief that the status of the general practitioner has gradually become lowered and that his position as a friend, counsellor, and confidant has greatly declined in the eyes of the public. This is a reflection on the medical profession as a whole, for it is by the standard of the general practitioner that the entire profession is measured. Several factors seem to have been responsible for this unfortunate state of affairs.

A Prime Essential

All the blame cannot be attributed to State intervention. The profession has also been at fault, and it is time that it should put its own house into order. This will need careful planning at both pre- and post-graduate levels. The first essential is to curb the incentive for specialization, which has been encouraged to an unreasonable degree. Without neglecting the purely academic side of medicine, many more students should be encouraged to aim at general practice as their ultimate goal. For this the student of to-day does require a period of training, which might best be given efficiently by selected general practitioners.

General practitioners of standing might be appointed, as necessary, to the staffs of teaching hospitals; here they could give special instruction in their own *métier*, and also arrange for domiciliary visits with the student in attendance. Common ailments constitute about 90% of all illness, and the management of these can be properly learned only by seeing the family doctor in action and following him on his rounds. Later, as a postgraduate, the student would undergo a period of apprenticeship with a G.P. in further preparation for his entry to the ranks of general practice.

Revision courses will be needed from time to time so as to keep abreast of recent advances in medicine. Too many young doctors are seeking higher degrees by the short cut of intensive study rather than by the long road of practical experience. Postgraduate diplomas obtained after a short period of study should not entitle a doctor to regard himself as a specialist. The measure of proficiency of any person should depend on his basic knowledge of generalities.

The G.P. should occupy a position second to none in the profession. Why should he be expected to regard the specialist as belonging to the highest ranks of our medical hierarchy? In general, the family doctor carries into practice the true Hippocratic approach to medicine with much more sympathetic feeling than the specialist, whose work confines him to a much more restricted field. "Where there is love of humanity there, too, is love of the art."

Nevertheless many G.P.s are discontented, and some would seek to enhance their position through the foundation of a new College of General Practice with powers of conferring higher degrees. There are some arguments for and against such a College, the chief objection being the risk of grading of the general practitioner, and causing a category of specialists within its own ranks. It is generally agreed that no doctor can adequately practise medicine to-day without hospital facilities, for a doctor in general practice who has not some access to a hospital is like "a carpenter without his tools." The doors of the hospitals should be freely opened to the practitioner, so that he can follow the progress of his patient and test his diagnostic skill at every stage of an illness. In some isolated localities it would seem highly desirable that the smaller hospitals should be staffed by general practitioners with specialists at their disposal.

Apart from the importance of prestige, a good deal could be done to lessen the burden of work which appears to be the lot of many general practitioners. Overwork and good medicine are mutually antagonistic. A doctor who has to keep too many records and to see too many patients must at times suffer from mental and physical fatigue. Sometimes he is driven to lessen the load of his manifold responsibilities by referring some of his patients with undue precipitancy to a specialist or to a hospital. The sharing of liabilities in this way often leads to delay in starting treatment, and personal touch with the patient may easily be lost.

Although much has been written about the plight of the general practitioner, too little has been said about the reactions of the patient under the influence of State-organized medicine. Of recent years broad changes have taken place in the attitude of patients towards their illnesses. They now often welcome, and indeed demand, full-scale methods of investigation and do not mind running the gauntlet of men and gadgets. While, up to a point, this outlook is desirable, it can be abused when patients avail themselves of a service which gives them the right to consult their doctors and consultants on the slightest provocation. There is also a fear that under a so-called free service some patients may become too introspective about minor ailments and that the trammels of imaginary ills and anxieties may become self-nurtured to an unreasonable degree. No one would decry the importance of minor disturbances of either the body or the mind, but factors which might tend to initiate, aggravate, or perpetuate them should be discouraged. The unnecessary direction of patients from doctor to doctor in a roundabout fashion may appeal to some of them, but others will be dissatisfied and lose confidence in the competency of their own medical attendant.

As the subject of State-organized medicine appears to be limitless, it is a relief to turn to medicine of a more congenial kind. The evolution of scientific medicine from the past to the present and to the foreseeable future has in recent years been the subject of many important addresses. I do not propose to go over this wide field again, but will limit myself to a few subjects which I think are worthy of our present consideration. I refer in particular to the comparatively new specialty geriatrics, to an older form of medicine now appearing in a new guise under the name of psychosomatic medicine, and to iatrogenic diseases, for which the doctor is mainly responsible.

Interest in Geriatrics

Medical and social progress in the past 50 years has greatly altered the age-group distribution of the community. The increased expectation of life, together with the general increase in the number of the population, has resulted in a high proportion of people over the age of 65. Population experts estimate that before another 20 years have passed there will be more people in Britain over the age of 65 than under 16.

To cater for this advanced age group, the study of gerontology has become intensified and the practice of geriatrics almost become a specialty. The medical profession must play a larger part in facing the problem of the ageing, which they themselves have helped to create. Geriatrics in a sense is the converse or mirror image of paediatrics, and in certain respects the problems are somewhat similar.

Ageing is an essential part of living, and it does not deserve the reproach that

> "When he is forsaken,
> Withered and shaken,
> What can an old man do but die?"

The medical and general care of the ageing, conducted along skilful lines, can provide a degree of comfort, relief, and happiness far beyond the expectations of our forefathers. Many elderly people are most useful members of the community, and in a social sense their proper care will pay ample dividends by restoring to usefulness some of those who otherwise might become a burden or a charge on their relatives, their families, or the State.

In the main, however, provision for the care of the ageing will be an increasing State responsibility in the form of additional pensions, social security measures, and early retirement allowances. In certain instances institutional treatment and accommodation will have to be provided: here charitable and philanthropic organizations can play an effective part. A large share of these expenses will have to be borne by the younger members of the community who have displaced their older brethren. But the younger generation must not be unduly exploited by its elders. In the struggle for existence youth will be served, and in competition against old age they must inevitably succeed; for

> "In the lexicon of youth, which fate reserves
> For a bright manhood, there is no such word
> As—*fail*."

At the same time let us not forget the song of the Psalmist, "Cast me not off in the time of my old age; forsake me not when my strength faileth."

Psychosomatic Medicine

There is really nothing new about the concept of psychosomatic medicine, for it is recorded that Socrates informed his countrymen that in one respect the barbarian Thracians were in advance of Greek civilization. For "they knew that the body could not be cured without the mind"; this, he continued, "is the reason why the cure of many diseases is unknown to the physicians of Hellas, because they are ignorant of the whole."

While admitting that there should be no dichotomy between the psyche and the soma in the causation and investigation of disease, there is a danger that enthusiasm for psychosomatic medicine may become exaggerated. One author has gone so far as to state that all medicine will be psychosomatic in the future. Many of us would dread the day if patients were referred to simply as psychosomatics.

We have ample evidence that some symptoms are unrelated to any structural organic changes and, *per contra*, that emotional factors can cause disturbance of bodily functions. Glandular secretions, vascular changes, and the mobility of certain viscera are certainly modified by emotional reactions, but there is no convincing evidence that emotional stress, *per se*, can initiate a disease process, although it may aggravate existing ones. To regard emotion as a major aetiological factor in the causation of disease would belittle the importance of bacterial infection, hormonal imbalance, and structural organic changes. Therapeutics applied on a psychosomatic plane with undue emphasis on the psyche can hardly commend itself as an enduring form of medicine. So, although the psyche and the soma are inseparable components, care must be taken to keep a proper balance and perspective between the two.

Psychosomatic medicine is not a specialty; it is merely a common-sense approach to the investigation and treatment of disease. It belongs mainly to the province of the general practitioner, who is able to assess and readjust any disharmony between the body and the mind in the great majority of his patients. A purely psychosomatic physician must be a *rara avis*, for how few can claim to be highly skilful both in psychiatry and in internal medicine at the same time?

Iatrogenic Disease

The meaning of iatrogenic disease is well exemplified in the pages of Axel Munthe's *Story of San Michele*, in which he wrote that "many were not ill at all, and might never have become so had they not consulted me." It is not sufficiently realized what harm doctors can do by creating the idea of imaginary illnesses in their patients, by injudicious remarks, lack of judgment, or undue emphasis on trivial complaints.

The type of patient who is particularly liable to iatrogenic disease is usually one with a nervous temperament who has an exaggerated or wholly unnecessary anxiety about his health. There are also some patients with a pessimistic

outlook who are susceptible to suggestions of an unfavourable nature. In the less nervous type of patient, anxieties which were previously non-existent may be aroused for which there may be no real justification. Once an anxiety has become fixed it is difficult to undo, particularly when it has been invoked through the instrumentality of the doctor.

The most fruitful source for the inception of iatrogenic disease is undoubtedly in the cardiovascular field. From time immemorial the heart has been the traditional seat of the emotions, so it is not surprising that cardiac neuroses often occur. It is difficult to define the term "cardiac neurosis"; presumably it means an exaggerated state of heart consciousness or anxiety unrelated to reality.

Although a cardiac neurosis is most frequently encountered in patients who have no cardiac disease, it also occurs in patients who have organic heart lesions. Indeed, in this latter contingency it is often of greater importance to treat the associated anxiety state than to concentrate too closely on the underlying organic condition.

The symptoms of a cardiac neurosis are very diverse and multiple, although a single symptom often predominates. Most commonly such patients complain of vague pain in the region of the heart, palpitations, breathlessness, faintness, and fatigue, but on careful analysis all of these symptoms may be inconsistent with actual heart damage.

It is therefore necessary that the doctor should be quite frank and positive in his statements, for uncertainty will never allay apprehension. He should be careful in his remarks about blood pressure, insignificant heart murmurs, and so forth, lest he make a cardiac cripple out of one who is structurally sound. For instance, preoccupation about blood pressure is often a constant source of trepidation with certain patients. The cardiac phobias are so common that Cabot in 1926 expressed the opinion that most heart disease is imaginary, and it is estimated that 40 to 50% of patients who consult a heart specialist are suffering from an exaggerated or unnecessary degree of anxiety about their heart. These phobias are often aroused or intensified by ill-considered or careless statements by the doctor concerning the integrity of a patient's heart.

Another precipitating factor is sudden or dramatic deaths among relatives or friends of the patient, although only a few varieties of heart disease carry with them the risk of sudden death. This was well known to our forefathers, for as far back as 1707 Lancisi wrote his celebrated work, *De Subitaneis Mortibus*, to allay the terror and alarm which had arisen in Rome in 1705 owing to the great number of sudden deaths in that year.

Teaching History of Medicine

While we may stress the recent improvements in medicine, we should not forget how much we owe to the physicians of the past. A great deal more attention should be paid to historical medicine; for, as Sir Henry Cohen has said, "a profession contemptuous of its own history runs grave dangers." Osler stated that by the historical approach alone many problems in medicine can be studied with profit.

Although one hesitates to add any further subjects to an already overloaded curriculum, I would make a special plea for the teaching of the history of medicine to students. This subject could be taught not only in the form of occasional lectures by experts, but more often also during the course of clinical instruction at the bedside.

If items of historical interest are presented in an attractive manner they will tend to enhance the value of the main discourse. It would be quite unnecessary to impose on the student the ritual or embarrassment of an examination in historical medicine; but his interest in the subject could be aroused so as to enable him, if he so wished, to explore a branch of medicine which presents many fascinating facets.

In this field of discovery and investigation one need not necessarily be an accomplished historian—in fact, the beginner with an inquiring mind can revel in the realms of historical research. For instance, although it is known that Oliver Goldsmith reviewed Auenbrugger's book on percussion, the *Inventum Novum*, in 1761, it would be more intriguing to discover why Rozière de la Chassagne's translation of 1770 was almost completely ignored until rescued from oblivion by Corvisart in 1808. Surely some surgeons would like to know more about the Irish Aesculapius, Diancecht, who treated the chieftain Nuada, whose arm was severed at the battle of Moytura, in Sligo, in ancient times. The emblem of the silver arm of Nuada now forms part of the presidential badge of the Irish Medical Association.

Medical Ethics

Another subject, of far greater importance, is the adequate teaching of medical ethics. Although there is a general code of honour which should govern the conduct of all men, there are special ethical standards which medical men accept and cherish as a necessary part of their calling. Medical ethics forms the foundation of our professional conduct and behaviour in relation to our patients, to the community, and between ourselves. It is not a selfish sort of code; it has primarily been designed for the benefit and protection of our patients.

On taking his degrees the medical student is often unpractised in the niceties of medical ethics because he gets too little instruction on its *modus operandi*. Teachers should bear this constantly in mind, and by example and by precept make the newly qualified man better fitted for the strict observance of basic ethical principles. Under the present-day forms of socialized medicine the traditional doctor–patient relationship is likely to be imperilled, to the detriment of both patient and doctor. There is good reason, therefore, why the teaching of medical ethics should hold a prominent position in moulding the character of the medical student, in whom lies the future integrity and rectitude of the profession.

The Years Ahead

One often wonders if the majority of students ever think in advance what particular branch of medicine they may be destined to follow. During their undergraduate career many students may be impressed by the accomplishment of others and may aspire to follow in their footsteps. Such wishful thinking can seldom be put to practical effect, for, although determination and perseverance may overcome many obstacles, these will not always compensate for lack of opportunity. This should not give rise to discouragement, for it often happens that a person who has ambitions to become a good surgeon turns out to be a better physician; and of course the converse holds equally true.

I have already referred to the idealism to become a good general practitioner, but I think the G.P. should in addition take a selective interest in some particular line of practice. Opportunities to do this often occur, sometimes in gradual stages and sometimes rather suddenly; but in either event he should be ready to meet the call when it comes. Interest in a subject may be aroused or stimulated from apparently trivial causes which, if followed up assiduously, may ultimately lead to a real vocation which hitherto had been dormant. I know of at least one instance where the reading of a single article inspired a doctor to take up a special branch of medicine.

Our younger graduates and undergraduates are so occupied with their academic studies that they have little time to examine the evolutionary changes which are taking place in medicine in the medico-political field. The British and Irish Medical Students Associations are becoming more alive to this problem, but they as yet hardly realize the significance of what is happening. The years ahead are full of perplexities and anxieties, for there is no doubt that medicine has now reached the cross-roads, to follow either the easy path of mediocrity and regimentation or the hard road of individual incentive and striving for perfection. The

choice can lie in only one direction if the profession is to retain an honoured place in the community. The British Medical Association, with its far-flung interests and its considerable influence, is well fitted and equipped to meet any challenge which threatens the rectitude of the profession. With unity of purpose, unshakable confidence, and sound medical statesmanship, success can be assured, for we yield to none in our devotion to our profession. Meanwhile

"Let us, then, be up and doing,
With a heart for any fate;
Still achieving, still pursuing,
Learn to labour and to wait."

FAILURE OF AN ANTIHISTAMINE DRUG TO INFLUENCE THE COURSE OF EXPERIMENTAL HUMAN BURNS

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In the *British Medical Journal* of July and August, 1951, a correspondence took place on the value of antihistamine drugs in the treatment of burns (Milne, Balfour, and Yeoman, 1951; Shubsachs, 1951; MacPherson, 1951; Levine, 1951; Slack, Boesen, and Husain, 1951; Laborit, 1951). Some of the writers gave the drugs by mouth, others as local applications in the form of creams. The favourable effects claimed included the relief of pain within a few hours of burning, the prevention or reduction of blistering and oedema, the prevention or reduction of infection of the burns, and an increase in their rate of healing.

If these claims are correct, antihistamine drugs should play an important part in the treatment of burns. However, we questioned their validity, since it had previously been demonstrated in this laboratory that various drugs used to protect guinea-pigs against the action of histamine had no detectable effect on experimental burns of various degrees of severity. The changes investigated in the guinea-pigs included erythema; capillary permeability; qualitative blood-flow changes in the skin, including stagnation and stasis of the blood flow; the clinical degree of oedema formation; skin sensibility; and the subsequent clinical courses of the burns (Sevitt, 1949a). Similarly, Weeks and Gunnar (1949), using rabbits, showed that pyribenzamine hydrochloride failed to alter either the increase of capillary permeability or the histological inflammatory picture after burning, although they claimed a reduction in the area of the post-burn erythema.

Nevertheless, negative results with animals do not rule out the possibility that antihistamine drugs may influence the course of human burns. We decided, therefore, to experiment on a group of human volunteers, each of whom would receive burns of the same severity and half of whom would take an antihistamine drug. By carefully observing the changes taking place in the burns, using clinical, photographic, and other methods, any significant differences between the two groups, such as those claimed in the *Journal* correspondence, should be noted. No such differences were found.

The Experiment

Burning.—Each of eight healthy male volunteers (aged between 27 and 41 years) received two small circular burns on the lateral surface of the left upper arm over the triceps muscle. The burns were spaced about 2 in. (5 cm.) apart, one above the other. They were inflicted by applying, with moderate pressure, the heated surface of a constant-temperature burning-iron on to the skin, which had been shaved the previous day. The iron was essentially a hollow brass cylinder closed at one end, which was the burning surface; it was similar to that previously described (Sevitt, 1949b) except that the burning surface was ½ in. (1.3 cm.) in diameter. A current of hot water, the temperature of which could be regulated and recorded, circulated through the iron. During burning the temperature of the iron was maintained at 60° C. and each period of application was 15 seconds. The temperature and duration of burning were selected on the basis of previous experience to give partial skin-loss burns (Bull, unpublished observations; Sevitt, 1949b). In this way two small circular burns of the same severity were inflicted on similar sites on each of eight volunteers.

Analgesia.—A few minutes before burning, the outline of a diamond-shaped area of skin on the outer surface of the upper arm was infiltrated with 1% procaine (without adrenaline), using about 25 ml. of solution for each person. By this means an area of anaesthetic or nearly anaesthetic skin was produced on which the burns were inflicted. Each subject found that the burning produced a little discomfort, particularly during the infliction of the lower burn.

Antazoline and Dummy Tablets.—The antihistamine drug used was antazoline (2-phenyl-benzyl-aminomethyl-imidazoline methane hydrochloride; "antistin"). This was chosen because it is readily available to the medical profession, has an efficient antihistamine action, and produces minimal side-effects. Antazoline (100 mg.) and dummy tablets were obtained in eight bottles, numbered 1 to 8, each containing 40 tablets. Four of the bottles contained antazoline and the others dummy tablets. The latter were similar in size, colour, shape, and taste to the former, but contained no antihistamine drug.* No one taking part in the experiment knew which of the bottles contained the antazoline tablets, and the bottles were allocated to the eight volunteers (which included the authors) by the drawing of numbered lots. In this way an attempt was made to avoid bias in the observations. Fourteen days after burning, when the main observations were completed, the key to the identity of the tablets was obtained from the manufacturers. The tablets were taken by mouth, the first one immediately after burning. The dosage was four tablets on the day of burning, and thereafter one tablet three times a day for the next eight days.

Confirmation of Antihistamine Action.—Skin histamine tests were performed on the seventh day, when the tablets were being taken, and on the twelfth day, three days after stopping the tablets. The tests were performed by pricking histamine acid phosphate, 1 g.% and 0.1 g.%, into the skin (Squire, 1950). Two pricks through each dilution were made on each forearm. The diameters of the wheals and flares produced were measured, and, by comparing the measurements obtained on the two occasions, three of the four subjects taking antazoline and three of the four con-

*We are informed that the composition of the dummy tablets was: quinine sulphate, 2.68 mg., lactose, 53.6 mg., starch, 83.6 mg., talc, 8.04 mg., and gelatin, 2.08 mg.

trols were correctly identified. The nature of six of the tablets taken was later tested by guinea-pig "protection" experiments. Half a tablet was ground up in saline and injected intraperitoneally, and an hour later 1 ml. of 1% aqueous Evans blue was injected intracardially. Skin histamine tests were then performed by injecting 0.05 ml. of histamine (1 in 1,000) intradermally. By comparing the sizes of the blue-stained areas around the injection sites it was possible to identify correctly five of the six tablets tested, three of which were antazoline and the remainder dummy tablets.

Dressings.—After each of the three observations in the first 24 hours each burn was covered with a 2 by 2 in. (5 by 5 cm.) sterile sheet of nylon, which was attached to the skin by strapping and then covered by a crêpe bandage. On the second day after burning this dressing was discontinued, and the daily dressing for the next seven days was penicillin cream on gauze covered with cotton-wool and secured by a crêpe bandage. This "closed treatment" of burns with penicillin cream (1,000 units/g. in "lanette wax SX") had the advantage of preventing the scabs from drying, becoming hard and adherent, and so interfering with the observations. Instead, the fibrinous exudate, called "pellicle" in this unit, remained moist and gelatinous and easily removable. When it was removed the underlying burn could be easily observed and photographed. During this time examinations and dressings were carried out with sterile precautions. From the ninth day onwards dressings were discontinued.

Recording and Examinations

The findings were recorded serially on eight charts, one for each subject. The chart headings included all the macroscopic changes which we have found may occur in burns. Those observed will be described later. The observations were made by two of us and often checked by others.

The burns were first examined 25 to 40 minutes after burning, when the skin anaesthesia had not yet worn off, and at three and a half to four and a half hours, when the skin sensibility had returned to normal. Bacteriological swabs were taken. The burns were photographed and covered with nylon dressings as previously described.

Next morning, 24 hours after burning, the burns were again examined, swabbed, and photographed. Blisters had now formed and blister fluid was removed by heparinized capillary pipettes from the burns of five of the volunteers. Total protein estimations were made by the micro-Kjeldahl method, and filter paper electrophoresis was performed to establish the albumin–globulin proportions.

The blister tops from all of the burns* were then cut away with sterile scissors and fixed in formol–saline for histological section. The exposed erythematous oozing bases of the burns were then examined, swabbed, photographed, and covered with nylon dressings.

Subsequent observations were made daily, except on the fourth day, until the ninth day after burning, when the penicillin dressings were discontinued. Photography and bacteriological swabbing were also done daily. Later examinations and photography were carried out on the twelfth, fourteenth, twenty-first, and twenty-eighth days.

Photography.—A special photographic bench was arranged to enable photographs on different days to be taken at the same distance and with the same lighting each time. In this way comparable photographs, using orthochromatic film and 35-mm. coloured transparencies (Kodachrome), were taken of the burns at each examination. In addition a few special "close-ups" were taken. Each photograph included a millimetre rule and serial identification number. To facilitate comparison of the photographs they were all enlarged to natural size.

Comparison of Burns on Subjects Taking Antazoline With Those Taking Dummy Tablets During the Stages of Acute Inflammation and Healing

Tablets Taken	Subject	Stage of Acute Inflammation					Stage of Healing			
		Clinical Oedema After Burning		% of Burn Area Distended with Blister Fluid 24 Hours After Burning	Blister Fluid Protein (g./100 ml.)	Time of Onset of Capillary Stasis (No Blanching)	Vascularization from the Periphery	Epithelization from the Edge and Base		
		½ hr.	4 hr.				Width of Peripheral Red Ring* (in mm.), 14th Day	Day Edge Epithelium First Noted (mm.)	Width of Edge Epithelium, 7th Day (mm.)	Day Burn Floor First Found Covered by Epithelium
Antazoline ..	A	+/+	++/++	60/60	Insufficient available	24 to 48 hours after burning	2·7/5·2	3/3	2/3	8/7
,, ..	B	+/+	+/+	80/80	5·8	,,	4·0/3·5	3/3	3/2	7/7
,, ..	C	+/+	+/+	100/100	5·8	,,	3·5/3·5	3/3	2/3	7/7
,, ..	D	+/+	±/±	30/60	5·3	,,	4·0/5·0	4/4	3/3	8/7
Dummy ..	E	+/+	++/++	100/100	5·0	,,	3·7/4·2	3/3	3/3	7/8
,, ..	F	+/+	+/++	20/10	Insufficient available	,,	4·7/3·7	3/3	3/3	8/8
,, ..	G	/+	/+	/20	,,	,,	/4·0	/3	/3	/7
,, ..	H	+/+	+/+	80/60	6·0	,,	3·5/3·7	3/3	3/3	7/8

NOTE.—(1) Numerals or signs to the left of the oblique strokes refer to the upper burns, those on the right refer to the lower burns. (2) The protein value from subjects B, C, E, and H are from the pooled blister fluids, that from subject D is from the lower blister. (3) Day 0 = day of burning; days 1, 2, etc. = following days. (4) ±, +, and ++ are degrees of visible burn oedema or blister distension.
* Calculated from the diameters across the inner and outer edges of the red ring.

Results

Before it was known which of the volunteers were taking antazoline tablets it was found impossible to divide the subjects into two groups according to the pathological and clinical findings. Some variations and differences in the burns were noted, but when the subjects were finally classified into antazoline and control groups the similarities and differences within each of the groups were much the same as the similarities and differences between the groups. The more important findings are summarized in the accompanying Table.

We have divided the changes in the burns into those which occur during the first 48 hours and those which occur later. The first 48 hours is the period of the acute inflammatory change, and, by inference from the H-substance theory of Lewis (1927), it is during this period that antihistamine therapy would most likely have beneficial effects. The later changes, including those of healing, will then be described, possibly in more detail than is necessary

*In one subject (G in the Table), later found to have been taking dummy tablets, the upper burn did not produce oedema and failed to blister. Only a localized area of blanching erythema developed, which faded in a few days without scabbing or ulceration. When this burn was being inflicted the temperature of the burning-iron fell from 60° to 59° C. (this was the only burn in which this happened), but whether the different features of this burn were due to this is difficult to say. This obviously superficial burn will be omitted from the analysis.

for the purpose of this paper. We feel, however, that the findings will be of interest to those concerned with the healing of burns.

Period of Acute Inflammation (First 48 Hours)

Pain.—As procaine-induced regional analgesia, which lasted about an hour, was used for the burning, early post-burn pain was not experienced by any volunteer. Pain was absent when the analgesia had worn off about an hour after burning. However, the early spontaneous pain after any burn usually disappears within a few hours, and the claims made that antihistamine drugs relieve burn pain may be due to lack of appreciation of this fact.

Flare and Oedema.—Half an hour after burning and after the first tablet had been swallowed—that is, before the effects of antazoline could be considered to have taken place—three of the antazoline and two of the control group showed well-marked "flares" extending 10 to 15 mm. beyond the edge of the burns. These had disappeared at four hours. Definite and approximately equal degrees of oedema were present in all the burns half an hour after burning. At four hours (Fig. 1) the oedema had increased in both burns of one of the antazoline subjects (A) and had decreased in both burns of another (D). Increase in oedema also occurred in both burns of one of the controls (E) and in the lower burn of another (F) (Fig. 2). In the remainder of the burns in both groups the clinical degree of oedema remained unchanged from half to four hours. Next morning, when the blistering was maximal, oedema of the dermis was slight or absent in all of the burns.

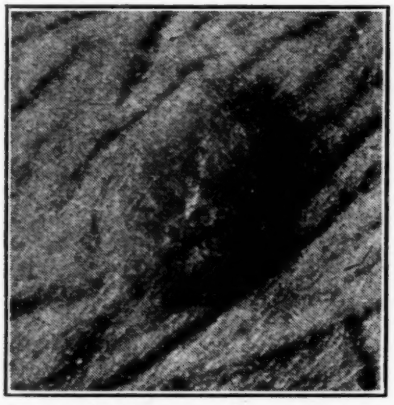

FIG. 1.—Subject A, four hours after burning and after beginning antazoline. The lower burn, showing considerable oedema. (Note: The irregular skin folds in Figs. 1 to 5 were due to the dressing. Figs. 1 to 7 are twice actual size, and Fig. 8 four times.)

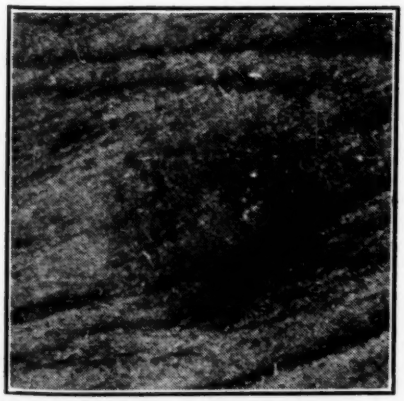

FIG. 2.—Subject F, control, four hours after burning. The lower burn, showing a well-marked oedema.

Blistering. — At four hours after burning, blistering was noted and was more definite in two of the antazoline subjects than in the remaining six volunteers. At 24 hours, blister distension involving 60% or more (Fig. 3) of the areas of both burns was present in three of the four antazoline subjects and in the lower burn of the fourth. Blister distension of similar extent (Fig. 4) was present in two of the four controls. In the remainder blistering was present, but the distended area involved 30% or less of the area burned (Fig. 5).

Blister Fluid Protein. — Sufficient fluid was aspirated from the blisters of three antazoline subjects and of two controls for protein estimations to be carried out. The protein content of blister fluid is a rough index of the permeability of the vessels in the underlying dermis. All of the fluids examined contained a high protein content, indicating a high permeability. For three of the antazoline group the values were 5.8, 5.8, and 5.3 g. protein per 100 ml. of fluid, and in the control group the two values available were 5 and 6 g. per 100 ml. Filter-paper electrophoresis showed that most of the protein was albumin, that α and β globulins were present, and that the proportions were similar to those found in normal serum. These findings do not suggest any difference in the degree of vascular permeability between the groups.

Histology of the Blister Tops.—Nearly all of the epidermis in every blister top was completely necrotic, and most of the blister tops contained the superficial thirds or so of a few hair follicles. Since either the whole thickness of the epidermis or the epidermis down to the deeper part of the Malpighian layer was present in each section, the site of blistering was either at the dermo-epidermal junction or through the deeper third of the Malpighian layer, or at both levels, in every burn. Differential white-cell counts were made of the cells in the exudate adherent to the deep surface of the blister tops. The haematoxylin and eosin sections were supplemented by sections stained with chromotrope 2R for eosinophil cells. The percentage of polymorphonuclear leucocytes was very high in all the exudates, varying between 91% and 95% of the white cells, the remainder being lymphocytes. In two of the antazoline subjects 1% of eosinophils was found: no eosinophils were seen in the other sections.

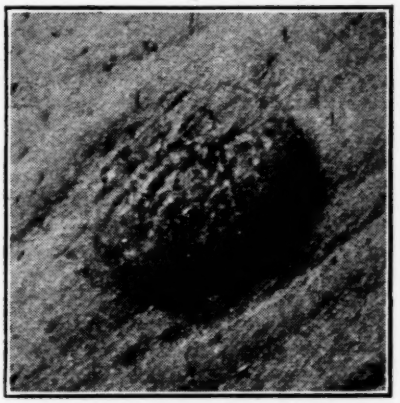

FIG. 3.—Subject B, taking antazoline. The upper burn, 24 hours after burning; showing a large distended blister. (Note: Blister formation varied within the antazoline and control groups. In each group large well-distended blisters (Figs. 3 and 4) and small often poorly distended blisters (Fig. 5) were formed.)

FIG. 4.—Subject E, control. The upper burn, 24 hours after burning; showing a large distended blister.

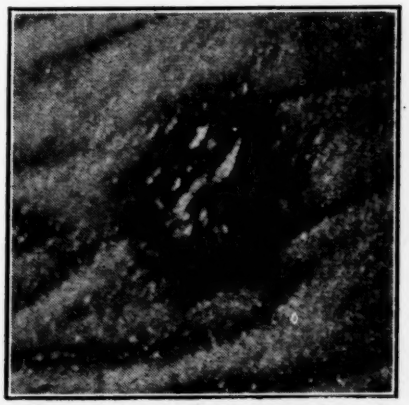

FIG. 5.—Subject D, taking antazoline. In the upper burn, 24 hours after burning, blister formation involved only about 30% of the burned area.

Erythema; Stagnation and Stasis of the Burned Dermis (see Table).—The blister tops were removed 24 hours after burning and the underlying dermis was exposed. In both antazoline and control groups the burns now appeared as localized pink or red raw areas oozing some fluid. When they were pressed with the edge of a glass slide the erythema blanched temporarily. However, the degree of blanching varied: in only one of the four volunteers in the antazoline group (both burns) was the blanching definite; in the remainder the blanching was slight. In two of the control group fairly good blanching was obtained; in the others the blanching was slight. At 48 hours after burning the erythema was still present in each burn, but blanching was now unobtainable—that is, stasis of the blood flow had set in. From these observations we may conclude that, 24 hours after burning, stagnation or retardation of the blood flow in the vessels of the upper part of the burned dermis had occurred in many of both groups of burns: at 48 hours the superficial local blood flow had ceased in all the burns.

Petechiae.—Small superficial petechial haemorrhages were seen in all the burns, and lasted a week or longer.

Peripheral Red Ring.—At 24 hours after burning a very narrow red ring was present at the periphery of the burned area in many of the burns. At 48 hours the red rings were quite distinct in all the burns, although only 0.5 mm. or less in width. Each one blanched well on pressure. These early rings probably indicate a lesser degree of vascular damage at the edges of the burns characterized by vascular dilatation without subsequent stasis.

Later Changes

Exudation

The gross appearance of an exudate from a burn depends on whether it is allowed to dry or not. If no dressing is used drying occurs and the familiar scab forms. If penicillin dressings are used and the burns are adequately covered, as they were from the second to the ninth day after burning in our series, any exudate formed appears as a gelatinous greyish layer lying on but not adherent to the burns. This wet form of burn exudate, called "pellicle" in this unit, consists histologically of a fibrin network containing fluid and numerous polymorphs. Pellicle was found in both groups of burns on the second and third days after burning. Thereafter the amount of pellicle was reduced: on the seventh, eighth, and ninth days either none was found or the amount was recorded as slight.

Healing

Healing of a partial skin-loss burn involved sloughing of the dead dermis or its invasion by a vascular granulation tissue, or both processes, and epithelization of the surface. It will be convenient to describe vascularization, epithelization, and sloughing separately.

Vascularization took place from the edge and from the base of the burns. Edge vascularization appeared early, beginning and progressing from the narrow peripheral red rings seen at 24 and 48 hours after burning. These rings progressively increased in width, reaching a mean diameter of 1.5 mm. in the 16 burns of the antazoline group and 1.4 mm. in the 15 burns of the control group on the seventh day (Figs. 6 and 7). The inner edges of the rings continued to move centrally, often irregularly in different sectors, so that the widths varied a little from sector to sector. In both groups the mean width of the rings was 2.7 mm. on the ninth day and 3.9 mm. on the fourteenth day, and the variations in width from burn to burn were similar in both series. After this the redness of the outer part of the rings began to fade and visible vascularization of the bases of these burns which did not slough (see below) appeared. By the fourth week the peripherally vascularized area had become normal in colour and the centres of the healed burns were erythematous.

Epithelization occurred both from the edge and from the base of the burns.

Edge.—In every burn on the third day a thin, *dry*, semi-transparent, whitish ring appeared at the inner edge of the peripheral red ring and measured about 0.5 mm. in diameter. That this was the first sign of epithelization was shown by its inward spread and thickening on successive days. On the seventh day the peripheral epithelial ring was about 3 mm. in width in every burn (Figs. 6 and 7). At first the outer part and later the inner part of this new epidermis became thicker, keratinized, and wrinkled when the skin was gently pinched. On the ninth day the edge epidermis reached a maximum width of about 4 mm. in diameter in most of the burns. By then, however, the remainder of each burn area had become covered by a thin sheet of epithelium which had presumably spread from epithelial elements in the base. On the fifth to the seventh day after burning careful examination of the central parts of the burns with a hand lens revealed the presence of tiny, whitish, less translucent foci slightly raised above the general level of the central area (Fig. 8). From these foci, often at the sites of regenerating hair follicles and presumably arising from them, the central burn area became covered with epithelium.

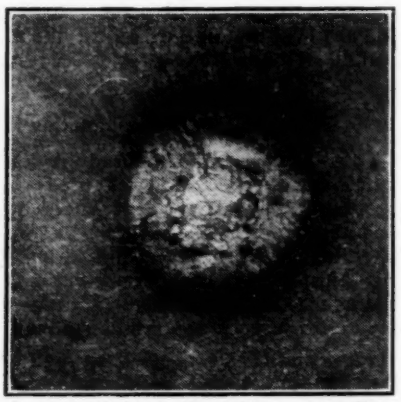

FIG. 6.—Subject D, taking antazoline. The lower burn, seven days after burning. (Note: In Figs. 6 and 7 each burn is surrounded by a narrow (1 to 2 mm. wide) red ring, which appears black in the photographs. This ring is due to vascularization at the edge of the burn, and within it is a ring of newly formed epidermis about 3 mm. wide. This, in turn, surrounds a central slightly depressed area containing tiny epithelial foci which can just be recognized in the photographs. The degree of edge vascularization and epithelization is about equal in the two groups.)

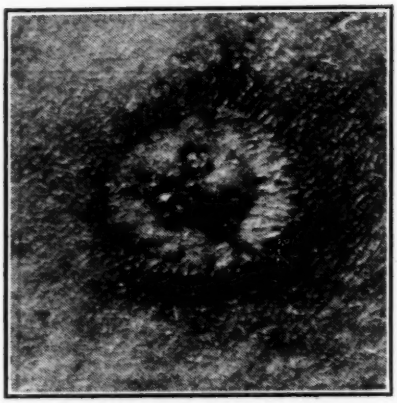

FIG. 7.—Subject E, control. The lower burn, seven days after burning.

Base.—On the seventh or eighth day the whole central area of each burn was seen to be completely covered by a thin transparent layer of epithelium drying after exposure to the air for a few minutes. Next day, or within the next few days, short hairs made their appearance, often in the centre of the epithelial foci. No difference was noted between the two groups in the times of first appearance of epithelial foci in the bases of the burns.

Sloughing and Re-epithelization of Epithelized Skin.—Within 48 hours of burning, the blood supply of the superficial dermis had ceased. The reddened base faded in colour and became whitish by about the fifth day after burning. This avascular and presumably *necrotic* superficial dermis was vascularized from the edge of the burn and was covered by epithelium arising from the edge and from hair follicles in the base. This was the situation on the ninth day, when the penicillin cream and dressings were discontinued and the burns were exposed. After this any exudate oozing through the thin unkeratinized epithelium

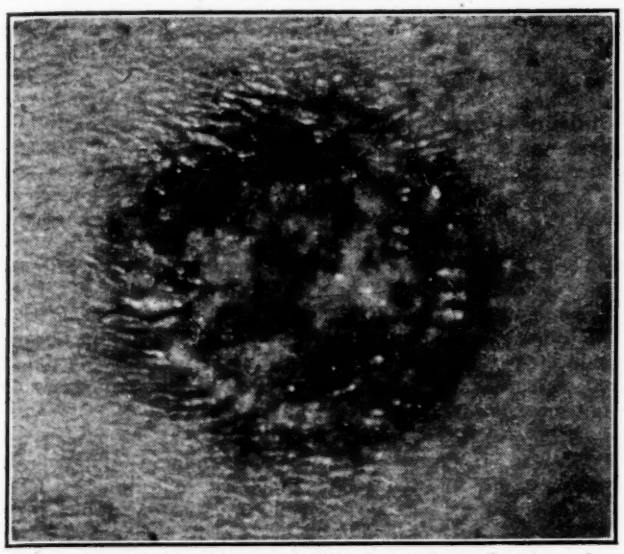

FIG. 8.—Subject D, taking antazoline. Lower burn, five days after burning. A number of tiny epithelial foci are present in the central two-thirds of the burn. For example, three epithelial foci are near the white reflection dots at the 4 o'clock position.

over the central part of the burns was allowed to dry and scab. In some of the burns in both groups, blood vessels invaded the superficial necrotic dermis and the surface epithelium continued to mature and to become keratinized. In more than half of the burns in both groups another process took place. In these, the white avascular superficial dermis dried into a brown scab about 1 mm. thick adherent to the base of the burn. Later, usually in the third or fourth week, the sloughs fell off or were easily removed, revealing red well-epithelized surfaces. One slough was sectioned and showed necrotic collagen with epidermis on both surfaces. It is probable that this sloughing was due to *drying* of the avascular dermis; that, instead of the necrotic dermis becoming incorporated into the healing burn as it commonly does (unpublished observations), a level of demarcation between the deep vascular and the superficial avascular dermis took place, and the latter sloughed. Epithelium spread once more at the line of demarcation, which became the new skin surface. Both processes occurred equally in the two groups, but in some subjects the two burns were affected in different ways.

Bacteriology.—Swabs of the cleansed skin taken just before burning produced a few micrococci from seven of the eight subjects and a few coliform bacilli from the other. Next day all the 15 blister tops were sterile, and swabs taken of both upper and lower burns during the next five days either produced no bacterial growth or contained only a few micrococci or diphtheroid bacilli. No difference was noted between the groups. The absence of colonization of the burns was probably due in part to the use of penicillin cream during this period.

Discussion

We have shown that there is no essential difference in the behaviour of small experimental burns of the same severity inflicted on four volunteers who took antazoline tablets and in four volunteers who took dummy tablets. During the acute inflammatory period of the first 48 hours both groups of burns gave rise to oedema of similar degree and duration; in both groups the area and distension of the blisters varied in a similar fashion; in both the histological level of blister separation, the concentration and nature of the blister fluid proteins, and the nature of the cellular exudate were very similar; in both groups stagnation and stasis of the blood flow in the vessels of the superficial dermis set in at about the same time. Spontaneous pain was not noted by any subject. The duration and, so far as could be judged clinically, the amount of exudate forming were the same in both groups. No real difference between the groups in the rate and manner of visible vascularization of the burns was found, and the epithelization from the edges and from the bases of the burns also occurred in a similar fashion in the two groups. Daily culture of the burns showed either no bacterial growth or very small numbers of saprophytic bacteria.

We can therefore conclude that the taking of antazoline within a few minutes of burning and its continuation in the dosage of one 100-mg. tablet three times a day had no effect either on the acute inflammatory changes during the first 48 hours or on the mode and rate of healing.

Procaine, however, was injected into every subject, and, since this drug has antihistamine properties, the possibility arises that the vascular changes might have been affected in *both* groups of burns and thus have weakened our conclusions. We believe this to be unlikely, because the antihistamine activity of procaine is weak and, if it took place, must have been short-lived in our experiment. This is supported by the observation that in five subjects well-marked flares developed around the burns within half an hour of the procaine injection and the burning.

Our observations demonstrate some of the variations which may occur even when burns are inflicted with a burning-iron at the same temperature and applied to similar skin areas for the same period. These variations may occur not only in different people but even in the same subject. Variations commonly occurred in the area and distension of the blisters and sometimes in the clinical degree of oedema. Later, rates of vascularization and epithelization also varied a little. If such variations can happen with controlled burns of the *same* severity, one can appreciate how difficult it is to draw conclusions from the behaviour of a series of accidental burns *varying* in severity, some treated with an antihistamine drug and others not so treated acting as "controls." Unless there is a great difference in the results of the treated and untreated groups no valid conclusions can be drawn.

Summary

Two small "partial-thickness skin-loss" burns were inflicted on similar skin sites on each of eight human volunteers. Each burning was carried out with a special burning iron at 60° C. applied for fifteen seconds. Four volunteers took antazoline tablets, starting immediately after the burns were inflicted and continuing (one tablet three times a day) for nine days. The other four took dummy tablets at the same time. The identity of the tablets was not known until the fourteenth day.

Observations during the first 48 hours were made on the clinical degree of oedema and its onset and disappearance; on the area and distension of the blister and the histological level of separation; on the concentration and nature of the blister fluid protein; on the nature of the cellular exudate; and on the time of onset of stagnation and stasis of the blood flow in the superficial dermis. Later, special attention was paid to the time of commencement, the rate, and the mode of development of vascularization and epithelization of the burns.

Although some minor variations and differences in the burns were found, the similarities and differences within both the antazoline and control groups were the same as the similarities and differences between the groups. We therefore conclude that the antazoline tablets failed to influence the course of the burns.

We acknowledge our thanks to Mr. L. Hurst, chief technician, and Messrs. J. Cooper and A. M. Hood, senior technicians, for allowing themselves to be burned and for their close co-operation; to Dr. J. H. Birch for performing the regional analgesia; to

Dr. C. Ricketts, for the electrophoresis; and to Miss S. Baar for technical help. Our thanks are also due to Messrs. N. R. Gill, C. Richardson, and M. Kirby, of the photographic department of the Accident Hospital, and to Mr. T. Stone for their skilled photography. Finally, we are grateful to Messrs. Ciba Laboratories Limited for supplying the antistin and dummy tablets and for their co-operation in the experiment.

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CONVERSION OF FOLIC ACID TO THE CITROVORUM FACTOR IN HEALTH AND PERNICIOUS ANAEMIA

BY

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In this paper the name "folic acid" is used collectively for all the substances in urine which stimulate the growth of *Lactobacillus casei* in microbiological assays; pteroylglutamic acid (P.G.A.) is used only for the pure substance. Citrovorum factor (C.F.) is synonymous with folinic acid, or leucovorin. The relation between these substances themselves, and between them and vitamin B_{12}, has been ably reviewed by Welch and Heinle (1951), and the reader is referred to their paper for more detailed references. There is reason to believe that in the body folic acid is converted to folinic acid, and that the latter is the form in which it acts. In the megaloblastic anaemia which develops in monkeys placed on a scorbutic diet the conversion of folic to folinic acid is impaired, and folinic acid is much more effective than folic acid in repairing the anaemia; the inability to activate folic acid in scurvy can be overcome by administering vitamin C (May, Sundberg, and Schaar, 1950). Callender and Lajtha (1951) found that folinic acid was more effective than folic acid in ripening human megaloblasts in marrow cultures, but the evidence collected by Welch and Heinle suggests that folic and folinic acids may be equally effective in the treatment of pernicious anaemia in man. It would therefore seem unlikely that pernicious anaemia is due to a failure to convert folic to folinic acid; but to obtain further evidence on this matter we have studied the excretion of folinic acid in the urine in health and in pernicious anaemia. It was already known that the oral administration of P.G.A. to normal men is followed by an increased excretion of C.F. in the urine (Broquist, Stokstad, and Jukes, 1951).

Methods

The subjects were 11 normal people, 8 patients with untreated pernicious anaemia, and 5 of the same group of patients after the anaemia had been treated. We measured the excretion of folic acid and C.F. in the urine during the first five hours after a dose of 5 mg. of P.G.A. by mouth. This period was chosen because earlier work (Spray and Witts, 1952) showed that the urinary excretion of folic acid after a dose of 1 mg. of P.G.A. by mouth was virtually complete in five hours. The excretion of folinic acid was also found to be largely completed in five hours in normal subjects after doses of both 1 mg. and 5 mg. of P.G.A. by mouth. The normal subjects were members of the department who were doing their usual work at the time of the test. The patients were confined to bed when untreated, but when the tests were repeated after treatment they were following their normal routine. Since neither age nor degree of activity appeared to affect the excretion of folic acid after oral doses of 1 mg. of P.G.A. in normal subjects (Spray and Witts, 1952), it was felt that the differences between the conditions in the different groups would not affect the results.

Urine for the 12 hours immediately before giving the P.G.A. was collected into a vessel containing toluene. All subjects were allowed a light breakfast, and about an hour afterwards they were given 5 mg. of P.G.A. in tablet form ("folvite") by mouth. Urine for the following five hours was collected into a fresh vessel. The volumes of urine were recorded, and samples were stored at 0° C. under toluene.

Folic acid in the urine was assayed with *L. casei*, using the same technique as previously (Spray, Fourman, and Witts, 1951). C.F. was assayed with *Leuconostoc citrovorum* in a medium containing acid-hydrolysed casein supplemented with glucose and various amino-acids, purines, pyrimidines, vitamins, and salts. The standards used for this assay were prepared by diluting a solution of the barium salt of the synthetic C.F. kindly sent to us by Dr. T. H. Jukes, of the Lederle Laboratories Division of the American Cyanamid Company. For both organisms the urine was diluted with water and added to the basal culture medium. Data for the recovery of added P.G.A. obtained from normal urine by this method have already been given (Spray and Witts, 1952), and Table I shows the recoveries of added C.F.

TABLE I.—*Recovery of Added C.F. from Normal Human Urine*

Urine from Subject No.	C.F. Added (mμg. per ml. Urine)			
	0·5	1·0	1·5	2·0
	C.F. Activity Recovered (mμg per ml. Urine)			
1	0·48	0·96	1·5	2·3
2	0·41	0·72	1·2	1·5
3	0·49	0·88	1·3	1·7
4	0·43	0·85	1·3	1·8
5	0·33	0·65	1·1	1·5
6	0·68	1·2	1·8	2·3
7	0·71	1·2	1·8	2·2
8	0·56	0·70	1·4	2·1
9	0·44	0·89	1·2	1·7
Means	0·50	0·89	1·4	1·9

TABLE II.—*Excretion of Folic Acid and C.F. in the Urine by Normal Subjects After 5,000 μg. of P.G.A. by Mouth*

Subject	Sex	Age	Folic Acid (μg. Excreted in 5 Hours)		C.F. (μg. Excreted in 5 Hours)	
			Before Dose*	After Dose	Before Dose*	After Dose
1	F	26	0·70	1,700	0·37	5·5
2	M	31	0·39	1,500	0·26	5·0
3	M	31	0·43	1,100	0·36	5·2
4	F	35	0·34	910	0·26	3·9
5	M	40	0·30	980	0·42	12
6	M	32	0·54	1,200	0·42	12
7	F	37	0·22	430	0·21	1·3
8	M	39	0·88	1,100	1·6	8·4
9	M	31	0·40	440	0·39	6·3
10	M	32	0·58	1,700	0·30	11
11	F	28	0·34	1,900	0·24	5·8
Means			0·46	1,180	0·44	6·9

* The values before the dose have been calculated from the excretion during the 12 hours immediately before the dose.

Results

Table II shows the urinary excretion of folic acid and C.F. in 11 normal people before and after the ingestion of 5 mg. of P.G.A. The folic acid figures have been corrected for the effect of C.F. on the growth of *L. casei*. Experiments showed that, weight for weight, C.F. was a little less than half (1/2.2) as active as P.G.A. for this organism. Between 8.6% and 38% of the dose appeared in the urine as folic acid in the first five hours, and there was a considerable increase in the rate of excretion of C.F., amounting to between about 1 μg. and 12 μg. in five hours.

Untreated patients with pernicious anaemia excreted significantly less folic acid than normal people under the same conditions. The output in the eight cases varied between 8.8% and 30% of the dose (Table III), the mean

TABLE III.—*Excretion of Folic Acid and C.F. in the Urine by Untreated Patients with Pernicious Anaemia after 5,000 μg. of P.G.A. by Mouth*

Subject No.	Sex	Age	Red Blood Cell Count (millions per c.mm.)	Folic Acid (μg. Excreted in 5 Hours)		C.F. (μg. Excreted in 5 Hours)	
				Before Dose*	After Dose	Before Dose*	After Dose
1	F	40	2·41	0·48	1,500	0·33	1·7
2	F	69	1·20	0·77	530	0·24	1·8
3	M	65	1·35	0·080	820	0·085	1·0
4	M	69	1·16	0·80	490	0·13	1·3
5	M	42	1·37	2·0	670	0·077	1·7
6	F	65	2·72	0·52	580	0·15	1·6
7	M	48	1·79	3·6	440	0·33	2·1
8	M	76	2·07	1·9	700	0·27	1·1
			Means	1·3	716	0·20	1·5

* The values before the dose have been calculated from the excretion during the 12 hours immediately before the dose.

being 716 μg., which is significantly lower than the normal mean of 1,180 μg. ($t=2.67$, $0.02>p>0.01$). These patients also showed an increased excretion of C.F., although the increase was smaller than in the normal group, never amounting to more than 2 μg. in five hours. In five of these patients who were examined again after treatment the excretion of folic acid after 5 mg. of P.G.A. by mouth became normal, and the excretion of C.F. also increased to within normal limits (Table IV). The mean excretion of C.F. in the five treated patients was 4 μg., which is not significantly different from the normal mean of 6.9 μg. ($t=1.80$, p slightly less than 0.1).

TABLE IV.—*Excretion of Folic Acid and C.F. in the Urine by Patients with Pernicious Anaemia in Remission after 5,000 μg. of P.G.A. by Mouth. These Data Refer to the Same Patients as in Table III, After Five or Six Months of Treatment with Vitamin B_{12} or Liver Extract*

Subject No.	Red Blood Cell Count (millions per c.mm.)	Folic Acid (μg. Excreted in 5 Hours)		C.F. (μg. Excreted in 5 Hours)	
		Before Dose*	After Dose	Before Dose*	After Dose
3	4·76	0·68	1,400	0·16	2·5
4	5·00	0·81	840	0·40	4·6
6	3·95	1·20	1,100	0·13	4·1
7	5·71	0·27	980	0·29	5·8
8	5·02	0·82	1,600	0·20	3·0
	Means	0·76	1,180	0·24	4·0

* The values before the dose have been calculated from the excretion during the 12 hours immediately before the dose.

Discussion

After an oral dose of 5 mg. of P.G.A. untreated patients with pernicious anaemia excreted significantly less folic acid than normal people or patients with pernicious anaemia in remission. This is in accordance with our previous results, using doses of 1 mg. of P.G.A. (Spray and Witts, 1952), and with the findings of earlier workers (Bethell, Meyers, Andrews, Swendseid, Bird, and Brown, 1947). All subjects also showed an increased excretion of C.F. after the dose, but the increase was much smaller in pernicious anaemia in relapse than either in health or in pernicious anaemia in remission. Even though the amounts of C.F. excreted after a dose of P.G.A. are several times greater than the resting value, they are so small in relation to both the test dose and to the excretion of folic acid that they permit of only tentative conclusions on the metabolism of folic acid.

At first sight it might appear that less folic acid is absorbed in pernicious anaemia and therefore less is available for conversion to C.F. This seems unlikely for several reasons. In our previous papers we have indicated that the diminished excretion of folic acid in pernicious anaemia is more likely to be due to increased utilization than to diminished absorption. Moreover, analysis of our experimental data shows that the variations in excretion of folic acid and C.F. are independent of each other. In other words, individuals with the lowest excretion of folic acid do not necessarily show the lowest excretion of C.F. Finally, the ratio between the amounts of C.F. and folic acid excreted is smaller in pernicious anaemia in relapse than in health or in pernicious anaemia in remission. This last finding indicates that there may be a defect in the conversion of folic acid to C.F. in untreated pernicious anaemia. An equally valid explanation, which covers all the facts, is that in pernicious anaemia in relapse the avidity of the tissues for folic acid is abnormally high, and that it is even higher for C.F.

Summary

The excretion of folic acid and the citrovorum factor in the urine after doses of 5 mg. of pteroylglutamic acid by mouth has been studied in 11 normal people, 8 patients with pernicious anaemia in relapse, and 5 of the same group of patients after treatment.

Untreated patients with pernicious anaemia excreted significantly less folic acid after the test dose than either normal subjects or patients with treated pernicious anaemia.

All three groups of subjects showed an increased excretion of C.F. after the dose, though in all groups it was seldom more than 1% of the folic acid in the urine. The increase was higher in most of the normal subjects and in the patients after treatment than in the patients when they were in relapse.

The results indicate that there may be a deficiency in the conversion of folic acid to the C.F. in pernicious anaemia in relapse, but they can be equally well explained by an increased avidity of the tissues for C.F.

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A team composed of two U.S. Army medical officers and a civilian physician left the United States on June 20 for Korea to investigate the value of dextran to be used with plasma under battle conditions. Dextran will not be used routinely in combat as long as the supply of whole blood and plasma is adequate to meet the demand. There is no substitute for whole blood, and plasma contains proteins, which dextran lacks. It is made primarily of sugar from molasses or beet juice. The U.S. National Research Council has investigated dextran clinically and authorized the Defence Department to stockpile it.

USE OF DEHYDRO*ISO*ANDROSTERONE IN PSYCHIATRIC TREATMENT

A PRELIMINARY SURVEY

BY

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Having noted the work of Hemphill, Reiss, and others on the relationship of "steroid" excretion to mental states, we decided to investigate the effect of dehydro-*iso*androsterone in selected cases of schizophrenia and "schizoid psychopathy." Our case-material was limited to patients who showed abnormal 17-ketosteroid excretion, to patients whose mental illness was mild or who were slowly deteriorating, and, as things turned out, to patients who gave the appearance of physical immaturity.

The group investigated in the first instance (Cases 1–5) consisted of males between the ages of 16 and 35 in whom the total 24-hour ketosteroid output, and particularly the alpha–beta ratio, was found to be abnormal. The normal 17-ketosteroid output for this age group in men is taken to be 6–21 mg. per 24 hours, of which the beta fraction constitutes 5–15%. Each case was independently investigated by at least two of the following: E. B. Strauss, W. A. H. Stevenson, and L. Rose, of St. Bartholomew's Hospital, and D. E. Sands, G. H. A. Chamberlain, and M. E. F. Woollaston, of St. Ebba's Hospital. The chemical investigations were carried out by A. M. Robinson at St. Bartholomew's Hospital and by W. W. Kay for St. Ebba's Hospital at West Park Group Laboratory. W. J. Tindall examined the first five cases and advised on the clinical and endocrinological aspects throughout. The last three cases (Nos. 6–8) are relevant and interesting in spite of the fact that it was possible to estimate the total ketosteroid output only—that is, without fractional differentiation.

Case 1

A man aged 33. Diagnosis, paranoid schizophrenia. Estimated duration of disorder, 14 years. Prior to this he had been a reasonably well-adjusted individual. The family history contained evidence of psychological instability and endocrine imbalance. Symptoms included incongruity of affect, outbursts of aggression, violent screaming attacks, and paranoid and other delusional ideas. Sexual interest had never developed. Previous treatment included hormone injections, psycho-analysis, and full insulin coma, without materially arresting the progress of the disease. Rorschach tests pointed to a diagnosis of paranoid schizophrenia. The total 17-ketosteroid excretion for 24 hours was 19.1 mg., of which the beta fraction was 7.5 mg.—an unusually high reading.

He received a total of 33 50-mg. (intramuscular) injections of dehydro*iso*androsterone, at first daily and later at longer intervals, and showed unexpected improvement after a few days. His final social adjustment appeared normal; he took up an occupation satisfactorily, and his outbursts became increasingly rare. He began to show some sexual interest. The Rorschach test was repeated after the twentieth injection; on this occasion there was no evidence of the more florid indications of schizophrenia, and the general picture showed a process of recovery. After treatment was completed his total 17-ketosteroid excretion was 18.7 mg., but it is to be noted that the beta fraction had dropped to the more normal figure of 3.5 mg. Some deterioration was noticed three weeks afterwards, but he was seen 17 months later, when his condition appeared much better than before treatment.

Case 2

A youth aged 17. Diagnosis, schizophrenia. Estimated duration of illness three years, with a marked predisposition and an unstable family history. Symptoms included mutism, repetitive actions, outbursts of violence, incontinence of urine and faeces, and bizarre postures. He was sexually inhibited. Previous treatment included electroplexy (E.C.T.) and deep insulin coma, without benefit. His total 17-ketosteroid excretion for 24 hours was 6.6 mg., the beta fraction being approximately 0.1 mg.—that is, below measurable limits.

He received a course of dehydro*iso*androsterone, beginning with 5 mg. on alternate days, whereupon his picture altered rapidly. He was shortly able to hold a conversation and describe his personal and domestic difficulties. There was a spontaneous outburst of emotion on one occasion (abreaction), after which he became sexually less inhibited. His condition at one time resembled hysteria rather than schizophrenia: there was a period of anorexia, and later he expressed great fear of recovery in case he had to return to his home situation; his toilet habits became clean. His condition later deteriorated, but not to its previous low level. He was eventually transferred to St. Ebba's Hospital, where investigations were continued by Dr. Chamberlain. At first his treatment was chiefly abreactive in order to cope with the presenting hysterical symptoms. It seemed that the psychopathology of this side of the picture was centred on his inability to face the home situation, the most difficult aspect of which depended on parental quarrels. He frankly expressed his preference for an ordered, sheltered, hospital routine. He was later given a course of deep insulin treatment, 32 comas in all, from which he appeared to benefit somewhat, in the sense that he talked more freely and for a while became more cheerful.

During the 15 weeks of abreactive and insulin-coma treatment he continued to receive 5 mg. of dehydro*iso*androsterone on alternate days. He was pleased when these injections were discontinued, since the good subjective results clashed with his overtly expressed desire for permanent stay in hospital. The clinical picture became progressively more schizophrenia-like and less hysterical—so much so that leucotomy was considered. The patient at first consented, but later withdrew his consent; nor were the parents agreeable. He left hospital in the care of his mother, but has since been admitted to another mental hospital.

Case 3

A man aged 24. Diagnosis, schizophrenia, with personality structure relatively intact. Estimated duration of illness 11 years, with rapidly increasing deterioration in the six months prior to his coming under medical care. Symptoms included impulses to assault people, blind rages, strong homosexual feelings, emotional impoverishment, a delusion that his life was guided by "beings" who made malign suggestions to him by signs and sounds. He had received no treatment apart from superficial psychotherapy. His total 17-ketosteroid excretion for 24 hours was 10.4 mg. with a negligible beta fraction.

He received a course of dehydro*iso*androsterone (10 mg. and 20 mg. on alternate days) and his mood and thought-content altered rapidly. After his first injection he experienced his first heterosexual feelings. He had been withdrawn, suspicious, and depressed, but now became exalted, grandiose, and overactive. Further investigations were carried out at St. Ebba's Hospital, mainly by Dr. Woollaston,

and his mental state showed some variability. In one phase he developed florid delusions of an ecstatic religious nature which did not appear to interfere with his prevailing mood of contentment. At other times he became tense and irritable, with destructive impulses which he usually managed to keep under control. He continued to receive dehydro*iso*androsterone injections for two periods of seven and six weeks respectively. The drug appeared to make him feel depressed and irritable and more subject to feelings of rage than at other times. His delusional ideas, which were originally mainly religious and ecstatic in quality, became frankly paranoid and unpleasant. Between these two courses of dehydro*iso*androsterone he was given 31 insulin comas and five electrically induced convulsions. The insulin was associated with increased excitement but produced no real benefit. On the suggestion of one of us (E. B. S.) stilboestrol was given in order to reduce the sexual desire (conscious and unconscious) to a minimum, but he refused to co-operate after four days. At the time of writing his mental state is still very variable, but the general picture is one of paranoid schizophrenia with expansive delusions.

His total 17-ketosteroids were estimated on 10 occasions, but the ratio between the alpha and beta fraction was not worked out. There appeared to be no correlation between his total ketosteroid output and his mental state at any given moment.

Case 4

A man aged 27. The differential diagnosis was as between a slowly progressive process-schizophrenia and post-schizophrenic defect. The duration of illness was difficult to assess. From the age of 18 onwards he had spent three years in an American mental hospital. His symptoms included timidity, apprehensiveness, ineffectiveness, diminished (almost absent) sexual awareness, strange mannerisms, paranoid ideas, and aggressive outbursts. He had been previously treated with endocrine and vitamin preparations: he had also had a course of insulin coma. The Rorschach and Wechsler tests tended to confirm the diagnosis of schizophrenia. His estimated I.Q. was 78. His total 17-ketosteroid excretion for 24 hours was 8.1 mg., with a negligible beta fraction.

We first treated him by means of injections of testosterone propionate. Daily doses in excess of 10 mg. tended to be associated with a desultory type of aggressiveness and purposeless overactivity, without any effect on the underlying schizophrenic picture. Treatment was discontinued for two months, by which time he had reverted to his habitual state of lethargy. We gave him a short course of dehydro*iso*androsterone (5-mg. injections). After three days he became more active and talkative. By the ninth day we had reduced the dose, as his response was tending to become excessive. As compared with the testosterone, it might be said that the beneficent mental change was more far-reaching and better integrated. This time he was able to discuss his personal problems, and developed a measure of self-criticism and ambition and more self-confidence. His ambitions were, however, beyond his capacity for achievement, and treatment was accordingly terminated. Some time later it was reported that he had remained more active and self-reliant.

Case 5

A youth aged 18. Diagnosis, schizophrenia simplex. Estimated duration of illness 10 years, with deterioration over the past two years. Symptoms included impaired concentration, indecision, thought-block, restlessness, depression, withdrawal, and a compulsion to imitate the undesirable actions of people in his environment. He had many tics and mannerisms. His pre-psychotic temperament was "hyperaesthetic schizothyme"—that is, quiveringly sensitive, lacking in drive, shy, and timid in social contacts. There was a family history of instability. He had received no previous treatment. His total 17-ketosteroid excretion for 24 hours was 9.9 mg. with again a negligible beta fraction—less than 0.1 mg.

He responded well to a course of dehydro*iso*androsterone. The picture improved as a whole: he gained more insight into his mental state; his mannerisms became markedly diminished; he became more confident and active; and his depression lessened. He would have passed for "normal" with the ordinary observer; however, his ambivalence was well beyond the limits of normality. Every impulse tended to be accompanied by its counter-impulse; and whenever any constructive plan was suggested he would automatically come forward with objections to it. He has been followed up over a period of eight months: improvement has been well maintained in spite of severe outside stresses.

Case 6

A man aged 22. Diagnosis, schizophrenia in an immature person who had recently been suffering from pulmonary tuberculosis. There was a one-year history of apathy and withdrawal, with self-consciousness to the point of ideas of reference—that is, a delusional conviction that people laughed at him. He found life "too complicated," and was mildly confused. He was of superior intelligence, but had always been a "lone wolf" type. There were indications, in the Rorschach test, of both generalized immaturity and schizophrenic tendencies.

The first ketosteroid estimation (July 30, 1951) was 6.5 mg. for 24 hours. A single injection of dehydro*iso*androsterone was followed by an immediate improvement. Progress was continuous throughout the course. After four weeks he became less tense, more animated and sociable, and less inclined to ruminate, with a corresponding subjective improvement. His total ketosteroid output had by then risen to 12.1 mg.

In November, 1951, it was decided to conduct a control experiment with the patient by substituting distilled water for the dehydro*iso*androsterone injections and later administering inert tablets. It is noteworthy that after two weeks a change for the worse was observed: he felt tired, weak, depressed, and so indifferent that he did not even bother to proceed home on leave. He recently restarted treatment with dehydro*iso*androsterone, and has once again improved.

Case 7

A man aged 29. The diagnostic label was schizoid psychopathy with obsessional features, together with general immaturity. He had always been sensitive, reserved, and shut in. For the past 14 years he had been odd, hypochondriacal, and given to obsessional preoccupations.

His total 17-ketosteroid excretion before treatment was 4.6 mg. for 24 hours. He was treated with dehydro*iso*androsterone for two periods of six weeks. The dose varied from 0.5 to 2 ml. (10 to 40 mg.) daily. Treatment was accompanied by a subjective improvement: he felt "warmer in mood," steadier, and less obsessional. This gain was only temporary—he relapsed when treatment was stopped—and there was no essential objective change. He is still under observation in the out-patient department.

Case 8

A man aged 22. Diagnosis, schizophrenia occurring in a person of striking generalized immaturity and retarded development. He had been rejected by his father and over-indulged by his mother. He had always been unusually egocentric. He told fantastic stories about himself and sought to be the centre of attention. Of late months he had become quite uncontrolled and given to outbursts of rage. He talked absurdly to complete strangers, and developed grandiose delusions of a quasi-religious nature. He gave a generalized impression of childishness.

His total 17-ketosteroids were within normal limits. The only effect of dehydro*iso*androsterone injections—even in a small daily dose of 0.5 ml. for five weeks—was to increase his tendency to rage and aggression. This continued for a while after the injections were stopped.

Results of Treatment

Roughly speaking, the results of treatment can be considered under two main headings, subjective and objective, although there is bound to be some overlapping.

Subjective.—Most patients stated that they felt less fearful and apprehensive and that the outside world appeared to be brighter and more real; there was an increase in self-confidence, combined with a slight euphoria; they felt more energetic and active.

Objective.—Behaviour-patterns became less withdrawn, and the patients seemed to be less apathetic and scared, and better adjusted to their environment. Their general attitude became manifestly more sthenic and virile. Those patients who had shown an undifferentiated or homosexual orientation began to develop heterosexual interests, although there were no observable changes from the anatomical point of view. Two patients became more accessible so far as analytical psychotherapy and rehabilitation were concerned.

Cases 2 and 8 became more deluded and paranoid, and so aggressive that treatment had to be discontinued.

Conclusions

It is clear that dehydro*iso*androsterone can alter mental states even in the case of schizophrenic illness of long standing. The chief effect of the drug would seem to be to increase self-confidence and to induce a slight euphoria. In the case of two patients, in whom delusion-formation was a prominent symptom, increased aggressiveness and nervous tension occurred in the course of treatment.

Further work will be needed to show whether these changes are in any way related aetiologically to the re-establishment of the normal spectrum of 17-ketosteroid excretion, either by substitution therapy as in Cases 2 to 5 or by suppression of an abnormality, as might explain the result in Case 1. It is perhaps noteworthy that all the patients mentioned in this paper were constitutionally immature, and more or less conformed to Kretschmer's description of pubertal retardation. In some cases the symptomatology resembled that of prolonged unresolved pubertal crises—again in Kretschmer's sense—rather than a true process-schizophrenia. These preliminary results suggest the possibility that the beta fraction of the 17-ketosteroids represents the metabolites of substances which may be concerned with the development of "self-confidence" in adolescence or early adult life, in a way somewhat similar to the adrenal stimulation of A.C.T.H. in raising resistance to general stress (Selye, 1950).

In the case of a drug with such positive results it is necessary to be very cautious in the matter of dosage and to vary the dose from patient to patient in accordance with constant psychiatric observation. Special prudence is demanded when aggression is present in the symptom-picture.

The results of treatment in this small group suggested that dehydro*iso*androsterone might be of value in the case of constitutionally inadequate and anxious juveniles, especially those with a tendency to schizoid psychopathy. Further investigations on these lines at St. Ebba's Hospital are reported by Sands and Chamberlain (1952).

We should like to acknowledge our indebtedness to Dr. E. F. Scowen, Dr. H. Crichton-Miller, and Dr. R. E. Hemphill, to all those who rendered assistance in this preliminary communication, and especially to Organon Laboratories for supplies of dehydro-*iso*androsterone.

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TREATMENT OF INADEQUATE PERSONALITY IN JUVENILES BY DEHYDRO*ISO*ANDROSTERONE

PRELIMINARY REPORT

BY

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Thirteen of the juvenile cases in the special unit at St. Ebba's Hospital for those aged 12 to 17 years have been distinguished by constitutional and emotional immaturity. Some were also intellectually dull. As a group they were inadequate, timid individuals, lacking confidence, and several were distinctly effeminate in attitude. They were physically small, looked younger than their years, and in two of the thirteen the genitalia were undersized and the testes incompletely descended. Eight were predominantly schizoid, three mainly anxious, one was a case of hysteria, and one an inadequate psychopath. In fact, such patients appeared to be the potential chronic schizophrenics or inadequate psychopathic personalities of early adult life. In view of the changes in mental state produced by dehydro-*iso*androsterone in a small group of young male adults of similar mental habitus, as reported by Strauss *et al.* (1952), it was thought possible that the drug might be worth a trial in this younger group, so lacking in development of the normal male confidence and assertiveness of youth.

By contrast, trial dosage of the drug was also given to four juveniles known to have aggressive trends. The average age of both groups was 15 years. Total 17-ketosteroid estimations were done in all but one case, though patients were selected on essentially clinical grounds. All patients had undergone the usual routine investigations and psychotherapeutic interviews for a month, and often more, before they received dehydro-*iso*androsterone.

The drug was given at first by injection only, the dose ranging from 0.5 ml. bi-weekly to 2 ml. daily—that is, 10–40 mg. No difference in effect was noticed when a change was made to oral administration in tablet form.

Specimen case histories are given below, but the general reaction to the drug was as follows. These patients were either schizoid, anxious, or inadequately psychopathic; and were characterized by feelings of inferiority, vagueness, timidity, apathy, and lack of social confidence. They mixed uneasily with others and at times were homosexual or effeminate. On giving dehydro*iso*androsterone no immediate changes were noted, but after a period which varied from four days to four weeks, according to individual differences and the size of the dose, the following type of response was seen to a greater or lesser degree in the whole selected group of thirteen cases. First, there was an increase in activity, showing as improved performance in school or occupational department and ability to discuss their feelings and future aims. Confidence increased, and at the same time timidity and vagueness diminished. Relations with their fellows became more normal, and in some who had been prone to homo-

sexuality the attitude became obviously heterosexual. There was little sign of any definite action on mood *per se*, but arising out of this swing towards better adjustment there was obvious contentment, with disappearance of depression. Weight was gained or maintained in all cases, but otherwise there was no noticeable physical change or maturation.

These changes are illustrated individually by the following four cases: two mainly schizoid, one chiefly anxious, and one inadequately psychopathic.

Case 1

A boy aged 15 was described as having been reserved, not mixing with other boys or fond of sports, but seclusive in his habits and given to excessive day-dreaming. He was inhibited and kept his thoughts to himself. In the past four years he had truanted, lost six jobs in the last few months, pilfered, lied, and become quite uncontrolled. His parents were divorced, and he had been deprived of parental care. After admission he appeared retarded, apathetic, and depressed. His intelligence was low average, and the E.E.G. doubtfully normal. The Rorschach test summarized him as immature, without affective response, and suggested early schizophrenia. In a few weeks he lost his depression, but continued to be emotionally dull and indifferent, though well enough to be tried at educational classes outside hospital. After eight weeks he gave up his classes and occupied himself with gardening in the grounds. On the whole he was more responsive and sociable, and was offered a suitable paid job locally. He soon again became more solitary and detached, and was found wandering outside hospital in a depressed, dazed state. When he had settled again he started routine work in the laboratory under supervision. He said that he liked strict supervision and feared to take any responsibility or initiative himself.

He was started on 20 mg. of dehydro*iso*androsterone on alternate days, rising to 20 mg. daily. Three to four weeks later he was seen to be more energetic, was working better, was more cheerful, and was mixing in games. His whole attitude and approach improved. After three and a half months on the drug he was able to discontinue it and to take up a factory job, which he has held for seven weeks without relapse. Though treated psychotherapeutically, the addition of the drug seems to be giving him the necessary confidence to make decisions and to hold a settled course in a contented way.

Case 2

A boy aged 14 was always regarded as a quiet detached youngster, shrinking from personal contacts, solitary, and effeminate by nature. During the past year he had been repeatedly truanting, though extremely self-conscious and oversensitive to criticism. He became preoccupied with the "psychology of religion," felt that he was "different," showed little emotional response, and was much absorbed with his own thought processes.

On admission he was vague and detached and gave long rambling explanations of his religious ruminations. He said that he felt empty, and at times laughed incongruously. He mixed with few other boys; and his odd manner persisted. A month after admission he was started on a course of dehydro*iso*androsterone, 1 ml. (20 mg.) intramuscularly on alternate days for nine weeks. After ten days he showed a considerable change, being more naturally self-assertive in manner and playing more readily with other boys; though he still discussed religion in a vague way, he was much more in touch with events. He had shown some homosexual trends, but these also disappeared during his treatment. Eventually he declared that he had lost his preoccupation with religious fantasy; and it was obvious that his social adjustment had greatly improved. In this condition he was discharged home.

Case 3

A boy aged 15 had been regarded as having a solitary type of make-up, prone to worry, to be preoccupied with the future, and to day-dream. He was much disturbed five months before admission, when his dog was destroyed; and after a subsequent attack of influenza became moody, disinterested, and depressed, with much irritability. He took six aspirin tablets and said that life was not worth living. He also attempted to suffocate himself with pillows. Physically he was undersized for his years, and appeared immature, with under-development of genitalia and pubic hair. To some extent he seemed to identify himself with his mother and her proneness to worry and over-anxiety. At first he was depressed and lacrimose, and had a number of physical symptoms. He showed improvement from the acute depressive reaction, but then appeared more frankly overanxious and oversensitive. He felt that he was a failure and worried over the opinions of others, with guilt over masturbation and feelings of sexual inferiority.

He was treated mainly by psychotherapy, but little real progress was made until he was given dehydro*iso*androsterone, 10 mg. twice a week. It was later felt that this dose was rather inadequate, since it was nearly eight weeks before he began to improve, to become more naturally aggressive, and to co-operate much better in psychotherapy and the discussion of his problems. Though more progress might have been made at first with a larger dose, it was certainly enough for him latterly, since he changed so much that on one or two occasions it was necessary to reprimand him for bullying other boys. After eleven weeks he was able to return home to his parents, and appeared to have recovered.

Case 4

This patient, aged 16, had been generally regarded as an immature sensitive youngster, with feelings of inferiority. He avoided boyish activities and often impressed others as being effeminate—enjoying knitting, sewing, and dressing dolls. He had few interests and in general was shy and reserved. Eighteen months before admission he began absconding from work and home, and stole a bicycle, subsequently returning it to the police.

On admission he appeared to be emotionally immature, though physically well developed. He was dull and childish, and handicapped by an over-indulgent mother and an indifferent father. Much of his thought was of a grandiose, wish-fulfilling type. He feared the onset of adulthood and its responsibilities. He wanted a nursing job, looking after children and babies. His mother's attitude had not helped him, since, while condemning him for childish sex explorations, she refused to discuss these matters with him in any enlightened way. He expressed dislike of the physical aspects of marriage. He was given 10 mg. of dehydro*iso*androsterone on alternate days for seven weeks; and after three weeks showed much improvement, being more lively, taking a leading rather than an inadequate part with other patients, losing his effeminate habits, and mixing normally with the opposite sex. As his social improvement increased he gained further confidence. He was discharged, much improved, after eight weeks, returning to his parents, having secured himself a job.

Other Cases

By contrast the drug was also given to four juvenile patients of a different type—three of schizoid and schizophrenic types and one psychopathic personality. All these patients showed aggressive features in their history, as opposed to the predominantly inadequate characteristics of the first group. On the same dosage as the latter, the aggressive psychopath of 18 years had to stop treatment after four weeks on account of the development of outbursts of rage and destructive behaviour, which settled a week after the drug was discontinued. During the past year he has never displayed aggression so intensively again.

A patient of schizoid personality with a history of aggression and attacks of temper became more alert and spontaneous after two to three weeks on the drug, but after six and a half weeks showed an increase of tension and aggression, attacked other patients, and had to be moved

temporarily to an acute ward. Another aggressive young schizophrenic showed an increase in impulsive, mischievous, and aggressive conduct two weeks after starting the drug. This phase continued for three to four weeks, though the drug was stopped four days after the change began. A paranoid juvenile schizophrenic case, not particularly immature physically or emotionally, became more acute with increased tension, attempted to smash a window, and required heavy sedation to relieve the situation.

Discussion

The most significant effect of dehydro*iso*androsterone is that it modified the behaviour of selected juveniles, and this effect was consistent in trend and form. Those who were socially and emotionally inadequate gained by becoming more normally confident, alert, and able to mix with their fellows. Those liable to be over-aggressive in mental make-up were made worse and appeared overstimulated by the drug. In both types the effect was temporary, since the "inadequate" patients, with two exceptions, tended to relapse, and the aggressive settled down to their usual state when the drug was discontinued. The presence of schizoid, anxious, or depressed features seemed to be of secondary importance in the selection of patients for this treatment, provided the inadequacy was present, as just described. Pending further investigation it can be said that dehydro*iso*androsterone acts as a form of replacement therapy, and that effective treatment is likely to be prolonged and the dosage varied according to individual needs. The usual range lies between 5 and 30 mg. or more, whether by injection or in tablet form.

Total 17-ketosteroid estimations, with two tests per patient, were performed in all cases. Irrespective of clinical type, half the patients proved to be within the average range for their age group and half were found to have low ketosteroid output in the urine. Estimation of total 17-ketosteroids was of little value in the selection of patients for treatment, which was done entirely on clinical grounds, as described. There is some indication, as noted in the paper of Strauss *et al.*, that selection may be possible through the fractional estimation of the 17-ketosteroid group. No alteration in primary or secondary sexual characteristics was noted. Dosage should be related to individual needs, not only for adequate treatment but to avoid complications.

The electroencephalogram was recorded in all but one case. The number of normal results exceeded the usual proportion for this age range in those admitted to the juvenile unit. No significant deductions could be made in this small series.

All cases had failed to respond to other measures before dehydro*iso*androsterone was begun. In this group of thirteen inadequate cases two recovered during treatment, five were much improved, three improved, and three others showed only temporary gain. None were worse, as happened temporarily in the four aggressive cases. Eight patients have been discharged.

Follow-up for the maximum of a year after the drug was stopped showed that of the thirteen patients only three have continued in their recovered and improved state, while the rest have suffered varying degres of relapse. It is obvious that in many cases the treatment will require to be prolonged over months to be of any lasting value.

While this treatment may replace certain factors lacking for normal constitutional endowment, it is not a substitute for proper psychotherapeutic investigation, though progress in psychotherapy can be accelerated through improved rapport. Furthermore, the gain in self-confidence enables many of these cases to take up the ordinary social and occupational pursuits of adolescence.

We are most grateful to Dr. W. W. Kay and to Mr. L. D. G. Hamilton, of the Mental Hospitals Group Laboratory, West Park Hospital, for their assistance and advice on 17-ketosteroid estimations; also to Organon Laboratories for supplies of dehydro*iso*androsterone.

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THE TREATMENT OF SJÖGREN'S SYNDROME WITH A.C.T.H.

BY

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In 1933 Sjögren described the ocular component of the condition which now bears his name, and which is becoming more widely recognized. It occurs mainly in middle-aged women, and consists of dry mucous membranes, parotid gland enlargement, and arthritis, though the syndrome is often incomplete. Kerato-conjunctivitis sicca is an essential part of the disease, and rhinitis sicca, xerostomia, pharyngitis sicca, and laryngitis sicca may occur. The lacrimal glands are involved but rarely palpable. In addition, an increased erythrocyte sedimentation rate, hypochromic anaemia, low blood sugar, achlorhydria, and alopecia have also been described (Weber, 1945).

A.C.T.H. has been used by us to treat two cases, and these are discussed below.

Case 1

A 60-year-old housewife was first seen in June, 1951, complaining of a dry mouth. Apart from some rheumatoid arthritis which began after the menopause at the age of 51, she had been perfectly well until March, 1948, when she had "influenza." She was kept in bed for a week with generalized aches and pains and loss of appetite, and immediately afterwards she noticed a wide variety of symptoms. Her sense of taste and smell disappeared, and her eyes became sticky and dry. Her mouth became very dry, making many foods difficult to chew, and she noticed that she was getting swellings near the angles of her jaw. These changed the shape of her face, seemed to vary a little in size, and were sometimes painful. Cracks developed at the corners of her mouth in June, 1950, but otherwise her symptoms had continued unchanged for about three years.

On examination each parotid gland was much enlarged but not tender, and she had severe rheumatoid arthritis with ulnar deviation in her hands. Her tongue was smooth, dry, and magenta-coloured, and her mouth was dry. There was an angular cheilosis, and she had kerato-conjunctivitis sicca. In addition there was a greatly enlarged liver and spleen, each being about five fingerbreadths below the costal margin.

A clinical diagnosis of Sjögren's syndrome was made, but the various laboratory investigations failed to reveal the underlying pathology or to account for the hepatic and splenic enlargements. Her plasma proteins were abnormal, in that she had a total of 9.2 g. per 100 ml., with albumin 3.55 g., globulin 5.65 g., and A/G ratio 0.63/1 by Howe's technique. Her gamma-globulin was 4 g. per 100 ml. (Cohn's technique), and no doubt this accounted for the abnormal flocculation tests, which were compatible with hepato-cellular damage. A liver puncture showed no abnormality of the liver cells, but one portal tract was filled with lymphocytes. The haemoglobin was 11 g. per 100 ml., with 3,700,000 red cells per c.mm. There was a neutropenia with a total of 2,000 white cells per c.mm. (280 polymorphs, 1,100 lymphocytes, 560 monocytes, 20 eosinophils, and 40 basophils). The sternal marrow was within normal limits, as were the blood-calcium, blood-phosphate, blood-sugar, urine, bleeding-time, clotting-time, and prothrombin-time estimations. The fractional test meal showed a low acid curve, and *x*-ray films of the hands and

shoulders showed typical changes of rheumatoid arthritis with some osteoporosis. Chest *x*-ray films and lipiodol bronchography revealed some left lower lobe bronchiectasis. The serum alkaline phosphatase was considerably raised at 75 units, and the E.S.R. was 29 mm. in one hour (Wintrobe).

Schirmer's filter-paper test showed moistening of the paper to 1.5 mm. in the left eye, and to 0 mm. in the right eye, as compared with a control of 20 mm., in three minutes, and the rose bengal test stained only the visible conjunctivae. No secretion could be obtained from either parotid gland, and a sialogram showed only very small intraglandular ducts.

In August, after a trial period on pilocarpine (with no change in salivation or sweating), she began treatment with a 100-mg. dose of A.C.T.H. daily by intramuscular injection. Within two weeks the parotid swellings had virtually disappeared, her liver and spleen were very much smaller, and her fingers were much freer. There was no improvement in salivation or in her eyes.

The A.C.T.H. was reduced gradually until she was getting 10 mg. once weekly and had had a total of about 4,000 mg. The treatment extended over six months, during which time her parotid glands, liver, and spleen, while varying a little from time to time, have remained more or less unchanged at their new small size, but there has been no improvement in the main symptom of a dry mouth. No substantial change was found on repeating the investigations, though the neutropenia has disappeared.

Case 2

A 54-year-old housewife was first seen in September, 1951, complaining of a dry mouth, sore eyes, and swellings at the angles of her jaw. She had been well until 1946, when she felt "run down"; a year later she was thought to be anaemic. In 1948 she was fitted with a complete set of dentures after the extraction of her last 10 teeth, and a few months later she noted that her mouth was dry, and that she had difficulty in chewing and swallowing solid foods. At about the same time her eyes became sore and she felt as if something was in them. A discharge would appear over the cornea, interfering with vision, and tears would not come even when she was crying or was peeling onions. Spectacles were prescribed without improvement.

In 1949 the parotid swellings were first noticed; there has been no fluctuation in their size since then, but occasionally they have been tender. Her condition continued unchanged until September, 1951, when she came into hospital, though she had been jaundiced for six weeks in 1950. She mentioned that her body hair had become scanty, and that she had sweated very little since the menopause in 1938.

On examination both parotid glands were enlarged and slightly tender; the orifices of Stenson's ducts on both sides were clearly visible. Some debris was present over the bulbar conjunctivae, and a little fluid was visible in the conjunctival recesses. There were rhagades around the mouth, and her tongue was dry and fissured. Heberden's nodes were present, but there was no other evidence of arthritis. Pubic and axillary hair was scanty, and the axillae were dry, but her palms and soles were moist. The rest of the examination was within normal limits, and a clinical diagnosis of Sjögren's syndrome was made.

Schirmer's filter-paper test showed moistening of the paper to only 3 mm., compared with a normal control of 40 mm., and the rose bengal test stained only the visible conjunctivae. Massage of the parotid glands produced at first a glairy mucoid fluid, and later a clear watery fluid with an amylase content of 9 units per ml. (normal 100–150 units per ml.). Although a slight increase in flow came after drinking lemonade, there was no response to pilocarpine or chewing paraffin wax, and iodide could not be found in the saliva after a dose of potassium iodide.

A liver puncture showed evidence of portal fibrosis, and the liver function flocculation tests were ++++, though the serum bilirubin and the serum alkaline phosphatase were normal. The peripheral blood picture showed a slight anaemia. The haemoglobin was 12.7 g. per 100 ml.; red cells, 3,500,000 per c.mm.; and white cells 3,000 (1,700 polymorphs, 1,000 lymphocytes, 250 monocytes, and 50 eosinophils). Some myeloid arrest was seen on sternal marrow examination, and there was a histamine-fast achlorhydria. Plasma proteins were 8.15 g. per 100 ml., with albumin 3 g. and globulin 5.15 g. (of which 1.9 g. was gamma-globulin) by Cohn's technique. The blood sugar, urea, potassium, sodium, chloride, calcium, and cholesterol were normal, as was the urine examination and the urinary diastase index. A sialogram was suggestive of chronic parotitis, but there was no sialectasis, and *x*-ray films of the chest, skull, and oesophagus were normal.

In October she began treatment with A.C.T.H. in doses of 100 mg. by intramuscular injection. The parotid swellings started to get smaller within a few days, and had disappeared after 10 days' treatment. Parotid secretion analysis showed an increase in amylase content to 38 units per ml., but there was no convincing improvement in the dryness of the mouth or eyes. The gamma-globulin fell to 0.5 g. per 100 ml., and the liver function flocculation tests were improved to ++. Myeloid arrest was no longer seen on repeat marrow films, and the leucopenia disappeared, but all other investigations previously carried out remained unchanged.

When the daily dosage of A.C.T.H. was reduced by stages to 20 mg., the parotid swellings slowly returned, and were again quite pronounced when the A.C.T.H. was stopped after 2,255 mg. had been given over 39 days. Because of this she was given 75 mg. of cortisone daily by mouth in the form of a syrup, and the glands once again regressed. After 750 mg. of oral cortisone had been given in 10 days, the drug was stopped and the patient was discharged.

She was re-examined six weeks later, in January, 1952. The parotid swellings had returned, though not to their original size, and she felt much improved in herself. The eye and mouth symptoms were unchanged, but parotid massage produced a larger amount of clear mucoid secretion with an amylase content of 43 units per ml. A stained smear of the secretion showed some mononuclear and epithelial cells, and a few polymorphonuclear leucocytes. The liver flocculation tests were again ++++, and the leucopenia had returned (polymorphs 2,250 per c.mm.), but there was no other change in the investigations, and the plasma proteins were not altered.

Discussion

The effects of Sjögren's syndrome may be widespread, but in most cases it is the parotid and lacrimal glands which are principally involved. The earliest change in the parotid gland is a disintegration of the glandular parenchyma (Sjögren, 1948). Later there may be atrophy, round-cell infiltration, connective-tissue proliferation, and fibrosis—all manifestations of a chronic inflammatory process of unknown aetiology (Ellman *et al.*, 1951).

In assessing treatment we must remember that the size of the parotid glands may vary spontaneously (Henderson, 1950). This may be due to intermittent blocking of the gland ducts, and at these times the glands may be tender and there may be a slight fever and malaise. However, neither of our cases had shown any marked spontaneous change in size before treatment began.

The disappearance of the parotid enlargements was very striking, though in both cases the swelling started to return when the A.C.T.H. dosage was reduced. In Case 1 small doses of A.C.T.H. over a long period controlled the swellings, while in Case 2 oral cortisone diminished the size of the glands while it was being given. Both patients felt better in themselves, but both said that their eye and mouth symptoms had not been improved. It was of interest that the size of the liver and spleen decreased in Case 1, and that the amylase content of the parotid secretion increased in Case 2.

There have been a few previous reports of similar treatment. Two cases receiving parenteral A.C.T.H. had at least a temporary increase in secretion and diminution in size of the parotid glands (Stephens, 1950; Frenkel *et al.*, 1951). Two other cases similarly treated failed to improve (Offret and Forest, 1950; Fitzgerald *et al.*, 1951). Cortisone used subconjunctivally gave no improvement in Duke-Elder's case (1951).

A temporary beneficial effect on the parotid enlargements has also been reported with deep *x*-ray therapy (Heaton and Shannon, 1948; Ellman and Weber, 1949). The response of the parotid enlargements to both A.C.T.H. and deep *x*-ray therapy is consistent with the presence of a chronic inflammatory lesion. However, this does not help us to identify the cause of the syndrome or to distinguish it from Mikulicz's syndrome, with which it is often confused, since this would probably respond similarly (Heaton and Shannon, 1948).

Summary

Two cases of Sjögren's syndrome are described, one of which had hepato-splenomegaly.

Treatment with A.C.T.H. reduced the parotid swellings to normal size, and the improvement was maintained as long as the drug was given.

There was no improvement in the eye and mouth symptoms.

We wish to thank Professor Sir Henry Cohen and Dr. E. T. Baker-Bates for permission to publish these cases.

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SUDDEN DEATH FOLLOWING AN INJECTION OF PENICILLIN

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Allergic reactions to penicillin are not uncommon—Keefer and Anderson (1950) placing them at 1.5–5% of patients treated—and are within the experience of most practitioners. Death due to penicillin therapy, however, is unusual and few cases have been reported.

When a fatal reaction does occur it seems to be due to (*a*) a Jarisch–Herxheimer reaction in known or unsuspected syphilitics; (*b*) severe allergic manifestations, usually occurring after a latent period and slowly progressing to death; or (*c*) anaphylactic shock producing death in a matter of minutes.

Of the few reported deaths attributed to penicillin, only one has been considered anaphylactic. Waldbott (1949) described a patient who, after receiving 50,000 units of penicillin intramuscularly during an acute attack of asthma, reacted immediately with swelling of the mouth, generalized itching, and collapse, with extreme cyanosis and death. She had had penicillin without ill effect several times before, but during the previous month had complained of urticaria and joint pains one week after penicillin therapy. Waldbott thought that the injection must have been intravenous.

O'Donovan and Klorfajn (1946), with an intramuscular injection of 15,000 units of sodium penicillin, produced an anaphylactic-like reaction in a patient known to be penicillin-sensitive. There was a slow recovery over the next two days. Non-fatal anaphylaxis was also reported by Burleson (1950) after the intramuscular injection of 200,000 units of penicillin with procaine.

Other fatal reactions attributed to penicillin sensitivity have been of a more prolonged duration, have frequently involved the skin, and have often occurred after a latent period, during which no signs or symptoms were noted. Thus a case described by Rabinovitch and Snitkoff (1948) developed a maculo-papular rash which progressed to exfoliative dermatitis and death seven days after the last injection of an eleven-day course of intramuscular penicillin. There was a family history of penicillin sensitivity.

Panja and Banerjee (1951) reported a case of an Indian woman who developed blisters of the lip and perineum after penicillin therapy, and who, four months later, had extensive bullae with exfoliation after streptomycin. The condition became very much worse and the patient died when the streptomycin was replaced by penicillin.

Barksdale (1946) reported a case of a sailor known to be sensitive to penicillin who, after his seventh desensitizing dose of 100 units of penicillin, developed a severe cutaneous eruption which progressed to a generalized exfoliative dermatitis, streptococcal septicaemia, and death. A case of Wilensky's (1946) received 30,000 units of penicillin four-hourly in the postoperative treatment of a subtotal gastrectomy. On the fifth day of convalescence the patient had a scarlatiniform rash which later became urticarial. There was a slow deterioration over the next few days, and death ensued.

Berne (1950) described a case in which there was an erythematous rash twenty-four hours after administration of sulphonamides and 30,000 units of penicillin in oil and wax. The condition progressed to an exfoliative dermatitis when the penicillin was repeated, in spite of the fact that the sulphonamides had been stopped. A repetition of the penicillin nine days later, when the skin condition had almost resolved, produced an acute flare-up, leading to generalized exfoliation, purpura, rapid deterioration, and death. Berne was able to demonstrate haemorrhagic necrosis of the bowel mucosa, with a primary lesion in the veins. Penicillin had never been given before.

The only case of fatal hypersensitivity to penicillin recorded in Britain occurred in a 14-months-old child who received "penicillin treatment" for a burn and who died five days later of serous exudation into the pleural cavities, pericardium, and peritoneum (*British Medical Journal*, 1951). Prior to death there had been a history of rash, pyrexia, and swelling of the face. It was not stated whether penicillin had been given before.

Chou and Welply (1949) reported a case in which death occurred two hours after the injection of 40,000 units of penicillin intrathecally as a prophylactic measure.

A case of sudden death following an injection of 300,000 units of crystalline penicillin is now reported.

Case Report

A man aged 67 entered hospital to have a bougie passed under an "umbrella" of penicillin and in conditions of rest. He gave a history of having contracted gonorrhoea in 1910, and of having attended a clinic for venereal diseases from 1930 in order to have bougies passed for a urethral stricture. With the exception of a short period in hospital with cystitis in 1940, bougies were passed at the clinic on an average of once a month until the date of his present admission.

On November 17, 1950, penicillin was given for the first time at the clinic. He received 300,000 units intramuscularly after the passage of a bougie. The type of penicillin was not stated on the clinic record, but it is presumed to have been crystalline penicillin G. This dose was repeated monthly during his routine visit to the clinic until May 4, 1951, when it was recorded for the first time that he received 300,000 units of procaine penicillin. Procaine penicillin was then given monthly until July 20. On August 24 bougies were passed and 300,000 units of procaine penicillin ordered. Immediately after receiving the penicillin intramuscularly the patient collapsed. He became unconscious and cyanotic, and was covered with a fine perspiration. There was a spastic contracture of one arm with deviation of the eyes. Within a short time he recovered consciousness sufficiently to answer questions.

On admission to hospital he was pale and had coarse rigors; he was conscious and had neither contractures nor paralysis. His pulse was rapid but of good volume. He was treated for shock and was discharged as well four days later.

There was no history of a similar occurrence following his previous injections of penicillin, nor was there a history of pruritus or urticaria. He had never complained of asthma, hay-fever, or other allergic condition, and there was no history of a hypersensitivity episode in the past. His Wassermann reaction was negative. He had attended his family doctor with myocarditis for several years, but there was no cardiac decompensation and he was a good worker. He was a heavy drinker, and it was learned that before attending the clinic he had had a hearty meal and had consumed a quantity of beer and spirits.

On September 28 he attended the clinic, where it was decided that a bougie would have to be passed. In the interval, while he had not been feeling in the best of health, he had had no localizing signs or symptoms and had had no skin eruptions. It was decided to admit him to hospital overnight so that he could be observed and the bougies passed the next morning. At this point, with the recent paper of Batchelor *et al.* (1951) in mind, it was thought that the procaine portion of the procaine penicillin had played a part in his recent episode and 300,000 units of crystalline penicillin G was ordered instead.

On the morning of October 5, after a quiet night without sedation and after a moderate breakfast, the patient was examined. He was slightly nervous, but, apart from occasional extrasystoles, the examination was essentially negative. His blood pressure was not taken, but his family doctor states that a recent reading was approximately 185/90 mm. Hg.

Ten minutes after the examination the patient received 300,000 units of crystalline penicillin G dissolved in 3 ml. of sterile saline intramuscularly while resting in bed. This was half of a total preparation of 600,000 units of penicillin dissolved in 6 ml. of sterile saline, the other half having been given to another patient immediately beforehand without subsequent ill effect.

Within a few minutes of the injection the patient began to feel nauseated and started to retch, producing a little vomitus. He became increasingly cyanotic, with shallow gasping respirations, and entered into a state of collapse. It was observed that his lips and tongue were swelling. At this stage his pulse could not be felt nor could his apex beat be heard. Adrenaline and nikethamide were administered without effect.

The cyanosis became intense, his tongue protruded, and there was slight frothing at the mouth. His breathing became progressively more shallow and infrequent, and death followed within a few minutes.

From the time of injection until death ensued not more than 10 to 15 minutes had elapsed.

Post-mortem Report

The relevant post-mortem findings were as follows.

Cardiovascular System.—A few small petechial haemorrhages were seen underneath the visceral pericardium. There was hypertrophy of the right ventricle, and two areas of myocardial fibrosis (2 and 1 cm. in diameter) were seen on the posterior surface of the heart. The coronary arteries showed intimal plaques of atheroma with narrowing of the left descending branch. There was no evidence of recent thrombosis.

Respiratory System.—Several small petechial haemorrhages were seen beneath the posterior visceral pleurae. There was evidence of chronic bronchitis and marginal emphysema. There was a basal congestion of the lungs.

Uro-genital System.—The bladder was hypertrophied, there was a granular cystitis, and a stricture was noted in the membranous urethra.

Central Nervous System.—There was a moderate degree of atheroma, with calcification of the circle of Willis and the basilar artery. A softening of the left cerebellar hemisphere (4 by 3 cm.) was seen.

Discussion

From the post-mortem appearances it is evident that the patient was a "poor risk" for any procedure, and it may well be that the shock of injection was enough to induce coronary spasm and an acute congestive cardiac failure. (The lesion in the cerebellum was proved histologically to be not of immediate origin.)

Clinically, however, the impression was that the phenomenon was anaphylactic in nature. In favour of this theory are the history and the character of his first collapse, the swelling of lips and tongue during his terminal episode, and the fact that the injection, not a new experience, was given under conditions of rest.

It is not sufficiently realized that serious and even fatal reactions may occur with penicillin therapy. Penicillin is still one of our chief weapons in the fight against disease, and it is prescribed daily, often indiscriminately, to large and ever-increasing numbers of the populace. Each year the number of people who have had previous penicillin therapy increases.

It is urgent, therefore, that the question of sensitivity be borne in mind before penicillin is prescribed. The increasing number of antibiotics becoming available for prescription makes the necessity for awareness of this phenomenon even more acute.

A past history of pruritus, urticaria, arthralgia, swelling of any part of the face, or rigors after an injection of penicillin should put one on guard. The delay between injection and reaction is often of some days and the connexion may be missed or misinterpreted. Previous injection of penicillin without ill effect is no assurance that sensitivity has not developed.

When in doubt intradermal skin tests should be carried out, patch tests to the skin being, according to the work of Wilkinson and Zinnemann (1947), not sufficient.

Summary

A case of sudden death following the injection of 300,000 units of crystalline penicillin is reported.

Some of the literature is reviewed.

Attention is drawn to the need to inquire carefully for signs of previous allergy before penicillin is prescribed.

My thanks are due to Dr. J. McGregor Robertson, consultant venereologist, Western Regional Hospital Board, for permission to publish this case and for helpful criticism, and to Dr. A. L. K. Rankine, physician-superintendent, Belvidere Infectious Diseases Hospital, Glasgow, for reading the manuscript. I would also like to thank Dr. W. A. J. Crane, of the pathology department, Glasgow Royal Infirmary, for carrying out the post-mortem examination.

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COMPARISON OF VASOACTIVE DRUGS IN MAN

BY

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The assessment of vasopressor drugs is commonly carried out in experimental animals under controlled conditions. Clinical trials follow, and if these are satisfactory the drug under investigation is added to the list of those already in use, and its properties are defined in terms of the results obtained by animal and human experiment. But, while the experiments in animals are fully controlled, those in the human involve many variables, and results in the latter tend to be coloured by findings in the former, regardless of the possibility of species differences.

In human trials it is desirable, therefore, to eliminate as many variables as possible, and at some stage in the investigation to try to reproduce the clinical conditions under which the drugs are most likely to find their greatest therapeutic application. Since individuals differ widely in their response to pressor drugs, this will involve comparing both of the drugs under trial in the same subject, unless very large numbers are concerned, as in a study by Dripps and Deming (1946) in which 2,500 patients were used to compare the effects of four drugs.

Under normal conditions homoeostatic vascular reflexes are at work which diminish the effects of injected pressor drugs, making it necessary to use relatively large doses in order to obtain a small response (Moe, 1948). Taylor and Page (1951) have shown that powerful components of these compensatory reflexes arise from chemoreceptors in the brain and have their efferent pathway in the sympathetic outflow.

In the experimental animal, stable conditions are efficiently obtained by destructive procedures on the central nervous system which eliminate vasosensory reflexes. Crimson and Tainter (1939) compared the effects of several pressor drugs in cats, in the normal state and in decerebrate shock, and found greatly augmented pressor responses after destruction of the central vasomotor mechanisms. Page and Taylor (1950) showed that a similar augmentation of vasoactive substances occurred after ganglionic blockade with tetraethylammonium chloride (T.E.A.C.), an effect which was intensified when elimination of T.E.A.C. was prevented by preliminary nephrectomy. The same authors found that preganglionic denervation between the sixth cervical and sixth thoracic segments produced the greatest pressor augmentation by local neural destruction.

In man temporary chemical interference with the compensatory vasomotor mechanisms can be obtained either by blocking the sympathetic outflow at the ganglion synapses, with drugs of the methonium group, or by the application of local analgesic to the appropriate sympathetic nerves. The methonium drugs are simple to administer but variable and evanescent in their effects, and are therefore unsuitable for providing a constant base-line of vascular hypotension against which the pressor effects of the test drugs can be measured. Of the nerve-blocking techniques available, subarachnoid and extradural spinal block are the most practical for routine use. Subarachnoid spinal block has a higher morbidity rate and a shorter duration of action than extradural block when administered by the single-dose method, and so the latter was preferred as providing the desired experimental conditions.

In this study conditions provided by depressed vasosensory reflexes have been illustrated by a comparison of the pressor effects of the two optical isomers of methyl amphetamine. The dextrorotatory (D-) form of methyl amphetamine is known as "methedrine" in English-speaking countries and as "pervitin" in Germany, and it is used extensively as a vascular and cerebral stimulant. The laevorotatory (L-) isomer is inferior to the D-isomer as a cerebral stimulant in animals and man (Hauschild, 1938), but little work has been done on the vasopressor properties of the L-isomer in man.

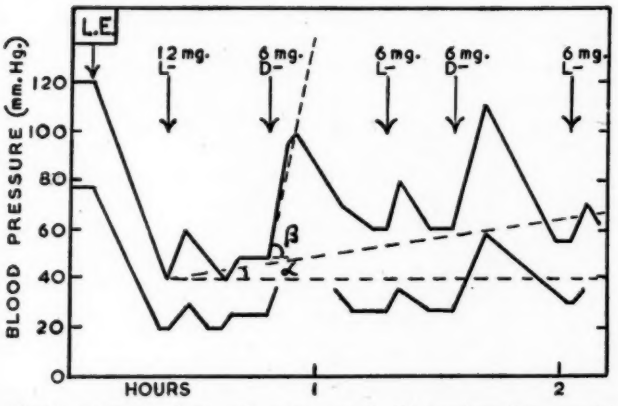
Method

Measurements were carried out on patients during routine surgical operations in which some degree of controlled vascular hypotension was thought desirable. No departure was made from the anaesthetic technique which would have been chosen irrespective of the investigation, and there was no question of treatment becoming subordinate to experiment.

High lumbar extradural spinal block was employed as part of the anaesthetic technique for 15 patients undergoing major abdominal or lower-limb surgery. A solution containing 1:600 "percaine" and 1.6% procaine was used, and injection made in any convenient space between the spines of the twelfth thoracic and third lumbar vertebrae. Dosage varied between 25 ml. and 45 ml., according to the height and age of the patient. Analgesia was carried to the upper thoracic segments so that the greater part of the sympathetic outflow was blocked, and the blood pressure fell to the region of 60 mm. Hg for a period of up to four hours (Bromage, 1951, 1952a). Alterations of blood volume were minimal, the total operative blood loss, estimated gravimetrically by weighing swabs, never exceeding 250 ml. in any one case. General anaesthesia was maintained with intermittent injections of thiopentone and inhalation of a mixture of one part oxygen and two parts nitrous oxide from a semi-open machine.

The limited time factor of a routine surgical operation made it impracticable to compare two pressor drugs of doubtful tolerance potentialities with a third drug, such as adrenaline, which is known to produce no tolerance effects on repeated injection (Chen, 1928). But errors due to tachyphylaxis were minimized by using small quantities

of drugs (Wislicki, 1949), and further control was obtained by alternating the order of administration of the isomers in successive subjects (Barger and Dale, 1910). Thirty milligrams of methyl amphetamine were dissolved in 10 ml. of distilled water, and intravenous doses of 6 mg. were employed after the blood pressure had become stabilized at a low level. Intervals of 30 minutes between injections allowed time for the blood pressure to rise and return to its base-line before administering the succeeding injection. In some cases the blood pressure did not return to its previous low level, but showed a slight increase following each injection of methyl amphetamine, the systolic base-line developing an upward drift. This may have been due to a cumulative action of the drug, or possibly to a retrogression of the epidural block, causing a progressive return of sympathetic innervation. For the purposes of this investigation errors due to drift of the blood pressure from an ideal horizontal base-line were ignored, because the slope of the drift was small (less than 15 degrees) compared with the slope of pressor response to injected methyl amphetamine (greater than 75 degrees), see Chart.



Blood pressure chart of man, aged 69, undergoing partial gastrectomy. General anaesthesia. Extradural block to T 2. $\alpha = 8\frac{1}{2}°$. $\beta = 79°$. The angle of drift of the base-line (α) is small compared with the angle of response to D-methyl amphetamine (β).

Results

Pressor responses to D-methyl amphetamine were found to be between nearly 3 and 15 times greater in the anaesthetized patient subjected to high spinal blockade than in the conscious normotensive subject (see Table).

Comparison of Systolic-blood-pressure Responses to D-methyl Amphetamine in Normal and Hypotensive States

Case No.	Age	Conscious Normotensive			Anaesthetized Hypotensive			Normal/Hypotensive Ratio
		Resting B.P.	B.P. Awake 2-5 min. after 6 mg. Meth.	Systolic Response (mm. Hg per 1 mg.)	Hypotensive	B.P. 5 min. after 6 mg. Meth.	Systolic Response (mm. Hg per 1 mg.)	
1	65	135/65	142/70	1·16	92/55	130/80	6·3	5·4
2	70	145/95	150/95	0·83	50/30	110/80	10·0	12
3	67	125/80	130/80	0·83	55/40	122/75	10·1	13
4	40	140/80	152/85	2·0	55/35	100/65	7·5	3·75
5	60	155/80	162/80	1·16	58/40	95/70	6·16	5·3
6	65	140/70	152/80	2·0	35/?	120/?	14·16	7
7	75	160/80	162/80	0·33	55/?	85/?	5·0	15
8	70	168/80	172/80	0·66	68/40	90/65	3·6	5·5
9	61	140/90	152/90	2·0	55/25	90/55	5·8	2·9
10	38	165/85	178/90	2·16	68/40	138/80	11·6	5·4
11	31	142/80	152/85	1·66	80/?	110/70	5·0	3·0
12	65	108/80	115/70	1·16	70/50	105/75	5·8	5·0
13	69	130/60	140/65	1·66	50/25	110/50	10·0	6·0
14	48	140/85	152/85	2·0	82/50	132/80	8·3	4·1
15	49	150/95	160/95	1·66	65/35	100/55	5·8	3·5

The pressor effects of dextrorotatory and laevorotatory isomers of methyl amphetamine were compared in 15 hypotensive subjects, and a total of 50 observations made—that is, 25 observations for each drug. The following results were obtained. *Intensity of Effect:* The L-isomer of methyl amphetamine is considerably less powerful than the D-form, the ratio of intensity being 1:2. *Duration of Effect:* The L- to D-ratio of their 50%-duration-times was 1:1.5. The absolute duration of effect of a small intravenous dose of D-methyl amphetamine under the conditions employed was of the order of 20–25 minutes.

Adrenaline.—The responses to L-adrenaline in the normal and in the hypotensive state were also compared in a small series. Single intravenous injections of 3–4 μg. produced either no change or a slight fall of blood pressure in the normal subject. In the hypotensive state under general anaesthesia a similar quantity produced a transient rise of 15–20 mm. Hg systolic pressure.

Discussion

The vasopressor drugs are most rationally employed in states in which vasomotor tone is defective, and so it is reasonable to assess their therapeutic merits under similar conditions. These conditions are found in patients subjected to sympathetic blockade for the purpose of controlled vascular hypotension in surgery. Under such circumstances most of the efferent pathways for homoeostatic vasodepressor reflexes are blocked, and a pure peripheral pressor effect is obtained in response to injected pressor amines. Thus small quantities of drugs produce easily measurable effects, and any tendency to develop tolerance is avoided.

At some point in any investigation a conflict is apt to arise between the interests of the patient and the demands of the experiment. It is felt that the technique outlined above resolves this conflict with the least interference to the patient. There is no need for a separate control series, since each patient is his own control, and the results are experimentally acceptable in a small series.

The considerable variation in degree of individual sensitization to pressor drugs in the unconscious hypotensive state, ranging from nearly thrice to fifteen times the normotensive response, may be referable to intrinsic factors of the individual response, or to the degree of anaesthetic interference with compensatory vascular reflexes, such as variations in the height of spinal block or depth of general anaesthesia. The first possibility is the most likely, since normal responses to a given dose of pressor drug vary widely from person to person. Furthermore, the upper limit of extradural block varied only between T 3 and C 8 in this series, and there seemed to be little correlation between either the initial level of hypotension or the percentage fall of blood pressure and the subsequent degree of augmentation of pressor response. However, the individual variability of augmentation is of no consequence in the comparison of two pressor drugs, since both drugs can be compared with fair accuracy in the same patient, and it is unnecessary to assess the drugs separately in two groups of patients. Indeed, if the latter were necessary the groups would have to be very large in order to reduce the statistical dispersion arising from individual variation within the groups.

The desirability of using controlled hypotensive techniques at all may be questioned. This subject is too involved to be discussed fully here, but certain remarks are relevant. The apparent harmlessness of these techniques, when used with the proper precautions and within certain limits, suggests that their use in the anaesthetized patient may not be so undesirable as would appear from experimental work on conscious hypertensive patients subjected to acute reductions of blood pressure. Kety and his fellow workers (1950), investigating cerebral blood flow in 17 conscious hypertensives, found that a 26% reduction of mean arterial pressure was accompanied by a 12% reduction of cerebral blood flow as measured by the nitrous oxide method, while cerebral oxygen consumption remained unaltered. In other words, demand exceeded supply, and the resulting cerebral oxygen deficiency was enough to cause anoxic symptoms of nausea

and vomiting in a proportion of the subjects. However, in the anaesthetized patient the situation is different. Schmidt (1950) and Wechsler *et al.* (1951) have shown that under light thiopentone narcosis cerebral metabolism is reduced by almost 40%, so that the relatively slight reduction of cerebral oxygen supply caused by hypotension is more than compensated by the greatly reduced cerebral oxygen demand. For this reason cerebral oxygenation would not appear to be jeopardized by the technique of controlled vascular hypotension, when combined with general anaesthesia, in either normotensive or hypotensive patients, provided anoxaemic anoxia is avoided.

Since this investigation was carried out observations made on the livers of anaesthetized patients suggest that the earlier recommendations for theoretically safe levels of controlled vascular hypotension are optimistic (Griffiths and Gillies, 1948). It has been found that anoxic reactions appear in the liver when the systolic pressure falls below 60 mm. Hg (Bromage, 1952b). For this reason the systolic pressure should never be allowed to fall below 60 mm. Hg except for very brief periods, and falls to the danger level should be corrected promptly by the administration of a pressor drug.

Summary

The sensitization to vasopressor drugs, arising from the blockade of central vascular control, has been studied in man by the use of general anaesthesia and high extradural spinal block.

It has been shown that a drug known to produce tolerance in moderate doses and even reversal of effect in large doses can be used effectively in the induced hypotensive state in repeated doses small enough to avoid the production of tolerance.

It is suggested that herein lies a valid method for comparing pressor drugs directly in man without the necessity for employing large series of cases. Such a comparison is illustrated by the pressor effects of the enantiomorphic isomers of methyl amphetamine.

I am indebted to Dr. W. A. R. Thomson for originally suggesting this investigation to me, and for his help in preparing this report. Supplies of D- and L-methyl amphetamine were kindly provided by Boots Pure Drug Company, Ltd.

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The waiting-lists for hearing-aids under the National Health Service are being steadily broken down, Miss Hornsby-Smith, Parliamentary Secretary to the Ministry of Health, stated at the annual meeting of the National Institute for the Deaf in London on July 4. She said: "I am glad to say that for some months past we have been able to supply the 48 distribution centres with all the aids they can handle, and more. There have, I know, been delays, but the shortage is now reduced to one of handling capacity and not supply. Some people have the strange idea that you can hand a deaf aid over the counter, as you would hand out a wireless set, but the fitting of a hearing-aid is a skilled and individual process, as there is immense diversity between the needs of the patients."

KARTAGENER'S SYNDROME

BY

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Although isolated cases had been reported by Siewert (1904), Oeri (1909), and Guenther (1923), Kartagener (1933a) was the first to call attention to the association of bronchiectasis and sinus maldevelopment with transposition of the viscera. He described four cases illustrating the triad. Later he reported seven further cases (Kartagener, 1933b; Kartagener and Horlacher, 1935) and since then the syndrome has been associated with his name. So far 82 cases have been reported in the literature, some of them having occurred in twins and siblings. These hereditary and familial tendencies of the syndrome were first noted by Guenther (1923), who reported the triad in two sisters among four siblings, and later emphasized by Kartagener and Horlacher (1935), Adams and Churchill (1937), Lopez (1944), Trogersen (1947), and Bergstrom *et al.* (1950). The cases described below occurred in two sisters with a strong family history of weak chest, and, although isolated cases have been reported, this, so far as I know, is the first time the syndrome has been observed in members of one family in this country. The father suffers from chronic bronchitis, and one brother, who could not be traced, is known to have a weak chest and when young was told that his heart was on the wrong side.

Case 1

A married woman aged 29 gave a history of recurrent upper respiratory tract infection followed at times by bronchitis for many years. Lately her cough had been much more troublesome and she brought up foul-smelling sputum, sometimes copiously. She had had pneumonia twice, and in 1940 a polyp had been removed from her nose.

Examination showed that she was a small woman of low mental grade, with short limbs and small hands and feet. There was no clubbing. She had dextrocardia, and the liver dullness was on the left side. Her lungs showed diffuse bilateral rales and rhonchi. The central nervous system was normal. A plain *x*-ray film of the chest was suggestive of bilateral bronchiectasis. An *x*-ray film of the sinuses showed that both the frontal sinuses were much smaller than normal. There was no evidence of infection. Situs inversus totalis was confirmed by barium meal. Unfortunately, the patient's husband objected to further investigations, and so neither E.N.T. examination nor bronchography was carried out.

Case 2

A married woman (sister of Case 1) aged 41 had always had a weak chest and had been subject to recurrent attacks of sore throat, nasal colds, and anosmia all her life. She had an attack of pleurisy at the age of 16, and in spite of the chronic chest trouble had been able to lead a normal life until recently, when her cough became more troublesome and the sputum more copious; the latter was blood-stained on two occasions. She also gave a history of increasing dyspnoea and swelling of the ankles in recent months. She had one normal healthy son.

On examination she was seen to be a small woman of low mental grade with adenoid facies, short limbs, and small hands and feet. There was moderate finger-clubbing. She had dextrocardia, and the liver dullness was on the left side. The lungs showed diffuse bilateral rales and rhonchi. The central nervous system was normal. Situs

inversus totalis was confirmed by barium meal and electrocardiographic examination. Sputum examination revealed a mixture of *Micrococcus catarrhalis* and streptococci. A blood count was normal, and the blood Wassermann reaction and Kahn test were negative. A plain *x*-ray film of the chest was suggestive of bilateral bronchiectasis, and the bronchogram was interpreted as follows: "The stem of the posterior bronchus of the right upper lobe shows dilatation, but the rest of the division is normal. The right lower lobe is grossly contracted and lingula is bronchiectatic. The inferior division shows cylindrical bronchiectasis, but the superior division is filled only in the proximal part. The left upper lobe is normal, but the left middle and lower lobes show a mild degree of cylindrical bronchiectasis."

The patient was seen by Mr. H. J. M. Stratton, who reports: "Nasal mucosa is pale and watery, with polypoidal fringes on both middle turbinates consistent with vasomotor rhinitis. Pharynx is healthy except for postnasal thick mucus. *X*-ray film of sinuses shows infection of antra and absence of frontal and sphenoidal sinuses and ethmoids. *X*-ray film of mastoids shows no development of mastoid air cells."

Discussion

Small frontal sinuses, or their entire absence, have long been regarded as a part of Kartagener's triad, but emphasis has recently been laid on other associated congenital abnormalities of the nasal sinuses. These features are well illustrated by my two cases. The first case shows the triad, whilst the second shows congenital abnormality of the paranasal sinuses to an extent which has been seen in only one previous case (Andrews, 1949). That case was later reviewed by Banham (1950), who points out that, as at birth the maxillary and mastoid antra are well-formed cavities and the frontal and sphenoidal sinuses and ethmoid air cells are underdeveloped, it would be interesting to know if this lack of development of the upper respiratory tract was always present in these cases, especially as previous writers have merely recorded absent or small frontal sinuses.

Coincidental occurrence of bronchiectasis, situs inversus, and congenital anomalies of the nasal sinuses is regarded as evidence of maldevelopment. In discussing the incidence of situs inversus totalis Adams and Churchill (1937) have shown that two types of people are affected by this maldevelopment—normal persons known as mutants, and those in whom the abnormality is associated with other congenital defects, known as monsters. They therefore classify sufferers from the syndrome as minor monstrosities. Both the above patients, besides showing the triad, were of small stature, with short limbs and small hands and feet, and were also of low mental grade, and I think can rightly be called minor monsters.

Another interesting feature of the syndrome lies in the possibility that a congenital defect of the bronchial wall is a primary cause of bronchiectasis. Infection of the upper respiratory tract and bronchial obstruction are usually regarded as important factors in the causation of bronchiectasis, but not all cases of bronchiectasis show evidence of both or even one of them. Moreover, Olsen (1943) has reported four cases of dextrocardia with bronchiectasis without sinus infection, and the very existence of this syndrome supports the theory that the weakness in the walls of the bronchioles is the primary factor in affecting their dilatation, perhaps aided by chronic infection. Farber (1943), in discussing the aetiology of cystic disease of the pancreas, postulated that there may be a constitutional defect of secretion in various glands throughout the body, and it is therefore suggested by Cohen *et al.* (1950) that bronchiectasis may be caused by inspissated tracheobronchial secretion, producing atelectasis and infection. Both my patients had chronic sinus infection, which must therefore be regarded as an important factor in the aetiology of bronchiectasis; but in cases without a history of upper respiratory infection or bronchial obstruction congenital weakness in the walls of the bronchioles must play a leading part in their dilatation.

Summary

Two cases of Kartagener's syndrome in members of one family have been observed for the first time in this country. They are here reported, and comments are offered on the extent of maldevelopment and on the aetiology of bronchiectasis.

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Medical Memoranda

Intolerance to Hexamethonium Bromide

Recent studies of the action of the hexamethonium and pentamethonium group of drugs on the gastro-intestinal tract and blood pressure will probably lead to their widespread use. It is therefore important that any idiosyncrasy or untoward action should be known, and with this object in view the following case is recorded.

CASE REPORT

A box-spring maker aged 53 had suffered from a duodenal ulcer for 25 years, otherwise his health had been good except for an attack of Bright's disease at the age of 7.

On January 28, 1951, he paid a routine visit to his doctor, who prescribed hexamethonium bromide for the relief of his ulcer pain, there being no history suggestive of pyloric stenosis. On the first day of treatment he took 0.25 g. before breakfast and lunch, and the following day increased each dose to 0.5 g., a total dose of 1.5 g. of the drug being given over two days. That afternoon, while watching a football match, he felt faint, vomited, and collapsed. After two to three minutes he recovered consciousness and felt very weak, but managed to walk home. He went to bed after further vomiting and slept. The next morning he felt better, but on arriving at work he again felt faint and collapsed: he lay down for a while and was finally taken home and put to bed. He continued to vomit throughout the day, and towards evening developed severe cramp-like pain in the calf muscles, which he described as "causing his legs to draw up." His doctor was called and he was admitted to hospital the following day.

On admission he was conscious and able to give a history, very lethargic and pale, but not cyanosed. His temperature was 98° F. (36.7° C.), pulse 94 and regular, blood pressure 65/49 (lying). It was impossible to take the blood pressure sitting up, as that position caused the patient to faint. No other abnormalities were found in the cardiovascular, respiratory, or alimentary system. Both pupils were dilated and did not react to light or accommodation; the central nervous system was otherwise normal.

It was considered that his condition was due to hexamethonium bromide. He was given 5 min. (0.3 ml.) of

1/1,000 adrenaline hydrochloride by intravenous injection and his blood pressure immediately rose to 125/65. However, within an hour it had dropped to 75/40; he was given an intramuscular injection of ephedrine hydrochloride, ¼ gr. (50 mg.), and it rose to 105/60. During the next day he was maintained on ephedrine hydrochloride 1 gr. (65 mg.) by mouth, and his condition was satisfactory, his blood pressure remaining about 115/75, although on sitting up it dropped to 70/60. From an absence of urine on the previous day his output rose to 66 oz. (1,870 ml.). From then on he continued to improve, although his pupils remained fixed and dilated for a further four days, and he remained on ephedrine by mouth for another week.

During his stay in hospital, routine investigation showed that his urine contained 6 parts per 1,000 of albumin but no casts or red cells. His blood urea was 142 mg. per 100 ml. and his blood bromide 30 mg. per 100 ml. It was thought at first that these changes might have been due to continued low blood pressure, but three weeks later his urine still contained albumin, his blood urea was 87 mg. per 100 ml., and a urea-clearance test showed a standard clearance of only 15% of normal. It is therefore more likely that his kidneys had already been damaged by his attack of Bright's disease. An electrocardiogram was normal. A barium meal revealed a considerable degree of pyloric stenosis, which was secondary to chronic duodenal ulceration as it did not show the characteristic picture produced by this drug.

COMMENT

It seems probable that this case represents true intolerance to hexamethonium bromide. A comparatively small oral dose produced a very marked effect which was prolonged over several days.

It is possible that the pre-existing renal damage might have interfered with the elimination of the drug, though without exact knowledge of its fate in the human body this would merely be a guess. Furthermore, it would seem unlikely, as hexamethonium bromide has been used in other cases with just as severe interference with renal function without producing such an alarming result.

This case does, however, suggest that small doses, probably no more than 120 mg. by mouth, should be used when beginning treatment with hexamethonium bromide, that the patient should be within easy reach of a bed, and that a careful watch should be kept on his blood pressure.

Our thanks are due to Dr. A. H. Douthwaite for his permission to publish this case and for his help and encouragement.

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Phaeochromocytoma Presenting as a Cardiac and Abdominal Catastrophe

In view of a report of a phaeochromocytoma presenting as an abdominal emergency (Gilliland and Daniel, 1951), it is of interest to record this very similar case.

CASE REPORT

A housewife aged 47 was admitted to hospital as a case of coronary thrombosis. She had a 12-hours history of sudden severe substernal and epigastric pain lasting half an hour, nausea, vomiting, sweating, and collapse. The attack had begun at 11 p.m. while strolling by the seashore. A local doctor recorded a blood pressure of 220/140 and a pulse of 160, gave her morphine, and asked for her to be admitted. The patient gave a past history of diabetes mellitus for over three years, stabilized at a Birmingham hospital at 20 units P.Z.I. daily, urine tests being done twice a year. She had had her insulin the day of the attack, but not on the morning of her admission. She had also had a similar but less severe attack of pain of a few minutes' duration three months previously.

On admission she was in an obviously shocked condition; pale and grey about the lips, cold, nauseated, and sweating profusely. Her temperature was 101.8° F. (38.8° C.), pulse 160, respirations 26, and blood pressure 60/?. The heart sounds were distant, with a soft apical systolic murmur. There was no abdominal tenderness or palpable tumour. The lungs and nervous system appeared normal. The urine was brick-red to Benedict's test and showed quantities of acetone, 1+ of albumin, and 8 g. of chloride per litre. Her haemoglobin was 113% and W.B.C. 12,500. She was put on anticoagulants and soluble insulin twice a day, with glucose feeds.

By the second day her blood pressure had risen to 140/80. She complained of encircling abdominal pains and appeared as shocked as on admission. Her abdomen was soft but tender in the left hypochondrium. The morning specimen of urine showed green to Benedict's test and no acetone.

On the third day she was found to have generalized extreme abdominal tenderness, some distension with gas, absence of bowel sounds, and a mobile mass the size of an orange to the left of the umbilicus. She said she had passed only a little flatus and no faeces since admission. A loud apical systolic and softer diastolic murmur had developed. Electrocardiograms showed no definite evidence of a coronary thrombosis but diffuse myocardial damage. *X*-ray films of the chest and abdomen were negative. Her haemoglobin was now 88% and W.B.C. 6.500. Her blood pressure was still 140/80, her pulse settled to about 120, and she remained slightly febrile.

A surgical opinion was obtained, but in view of her critical state and the likelihood of a coronary thrombosis no interference was recommended.

For the next ten days her general condition remained practically unchanged; the abdominal pain passed off but the distension remained; occasionally bowel sounds were audible and a little flatus was passed. Enemata and flatus tubes had little effect. The mass moved to the right of the umbilicus and became more palpable. The diastolic murmur vanished and the character of the systolic murmur changed. Meanwhile difficulty was experienced in stabilizing both her diabetes and her blood prothrombin time. She could take only small quantities of fluids by mouth, even through Ryle's tube, without vomiting, and finally an intravenous drip was set up.

Her blood pressure was 125/80 on the ninth day, rose to 200/110 on the tenth day, and fell to 180/80 by the twelfth day. She sweated a great deal during this phase. On the twelfth day she passed three motions and the distension disappeared, but next day she complained of severe pain in the left chest, had an epistaxis, became dyspnoeic, and died after a short period of Cheyne–Stokes respiration.

Pathology.—At necropsy (Dr. J. A. V. Morgan) all organs were found to be normal except the lungs, which were congested and oedematous, and the left suprarenal, which "was replaced by a soft encapsulated haemorrhagic tumour 8.5 cm. in diameter with a cystic centre. There had been a recent haemorrhage into the capsule of the tumour and the compressed tissues surrounding it. The left kidney was compressed and grossly distorted by the growth." Histology showed mainly necrotic matter with areas of cells compatible with those of a phaeochromocytoma.

COMMENT

As with the case of Gilliland and Daniel, there was much conjecture over the diagnosis of this case. The substernal pain and fall in blood pressure made a coronary thrombosis

seem most likely, with a mesenteric infarct to account for the second-day ileus. Phaeochromocytoma was considered because of the glycosuria and hypertension, but, after perusal of the papers by Crowther (1951) and Swan (1951), was rejected as unlike any previous case so far reported at that time. Unfortunately, the paper of Gilliland and Daniel was not noted until the day of the necropsy, when the similarity in presentation and signs was remarked upon.

Presumably haemorrhage into the cystic, friable, necrotic tumour produced the severely shocked state which, with a curious lividity of the skin, persisted throughout the whole illness. The use of anticoagulants must have aided this considerably, as must the bout of hypertension. A troublesome feature of the case was the diabetes, more and more insulin being required to keep the urine clear of sugar as her blood pressure rose after the original fall.

I would like to express my thanks to Dr. J. C. Prestwich for permission to publish this case, which was under his care.

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Phaeochromocytoma Simulating Thyrotoxicosis

In spite of a growing literature of case reports and methods of investigation, the diagnosis of phaeochromocytoma presents many difficulties, and it is probable that only a minority of cases are recognized during life. This state of affairs may be attributed to the apparent rarity of the tumour and the wide range of symptom-complexes it may produce. The tumour itself is often too small to demonstrate by physical methods, and other investigations may yield ambiguous results. The following case illustrates the similarity which may exist between thyrotoxicosis and the syndrome of hyperadrenalism.

CASE REPORT

A married woman aged 58 was referred to hospital on June 19, 1950, by Dr. G. C. Campbell, who suspected thyrotoxicosis. For 12 months she had suffered from paroxysmal vertigo associated with tinnitus and deafness on the right. More recently she had lost weight and complained of weakness and apprehensiveness. Her appetite remained excellent. There had been amenorrhoea since the normal birth of her second child 28 years before. Her previous health had been good. There was no family history of goitre and none of deafness.

Of slight build, the patient was evidently emaciated. Her weight was 5 st. 10 lb. (36.3 kg.). She wore a rather strained expression and was pale, but not obviously anaemic. Her hair was fine; the eyebrows and axillary and pubic hair were scanty. There was an impression of restlessness about her movements, which were rapid and bird-like. Other features were a resting pulse rate of 120, a blood pressure of 180/100, an apex beat in the sixth left intercostal space in the mid-clavicular line, and a loud systolic murmur heard over all areas and maximal at the apex. No exophthalmos was evident. There was a fine tremor of the outstretched fingers. The thyroid gland could not be felt. Examination of the patient's abdomen revealed no abnormalities. She was mildly breathless at rest, but no physical signs were found over the lung fields. The nervous system appeared normal apart from some nerve deafness on the right. The tympanic membranes were healthy and intact. The urine contained neither albumin nor sugar.

A threefold diagnosis of thyrotoxicosis, old rheumatic heart disease, and possibly otosclerosis was made. Mr. Arnold Gourevitch kindly saw the patient and agreed that thyrotoxicois seemed likely. At his suggestion an *x*-ray film of the thoracic outlet was taken. This showed no evidence of a retrosternal goitre.

On July 13 the patient was admitted to hospital, and on the 17th she was given methyl thiouracil, 600 mg. daily, and iodine. By July 23 she was able to say she felt much less agitated, but the pulse rate seldom fell below 100. Iodine was discontinued on July 27. By August 4 her condition was clearly not responding in the manner anticipated. Tachycardia and tremor persisted. On August 11 the pulse rose to a sustained rate of 150 and breathlessness increased. Venous engorgement appeared in the neck. The pulse rate was 170 on August 14. The pupils were constricted and the skin was moist. The blood pressure had fallen to 116/96. Methyl thiouracil was discontinued. On August 17 the patient was semi-conscious, pulse 120, and B.P. 100/70. On the 21st consciousness returned for a few hours, pulse 110. Death occurred on the 22nd.

Dr. A. G. Marshall conducted a necropsy, and I am indebted to him for the report, the positive findings of which were: "Thyroid 34 g. Smooth encapsulated surface. Cut surface showed excess colloid with no adenomata. One or two very small haemorrhages present. Lungs: gross emphysema with severe engorgement. Pericardial effusion (about 3 ml. clear yellow). Heart: no dilatation, no hypertrophy. Mitral valve moderately distorted, with thickened chordae tendineae, and clusters of small fibrinous vegetations on it. Other valves normal. Myocardium normal. Coronary arteries: double orifice of left. No atherosclerosis. Aorta: slight sclerosis. Stomach: engorged, containing altered blood. Liver: severely engorged. Adrenals: right, 6 g. normal; left, 20 g. Sections from the left adrenal show it to be composed of cords and columns of polyhedral cells with much cytoplasm and small nuclei. It is highly vascular, but there are no features to suggest malignancy. The appearance is highly reminiscent of the adrenal medulla. Unfortunately, as the tumour was unsuspected, no fixative agent containing chrome salts was available, and specific staining has failed."

DISCUSSION

In one of two cases of phaeochromocytoma recorded by McCullagh and Engel (1942) a similar error of diagnosis was made and death took place shortly after thyroidectomy. In this case the diagnosis of thyrotoxicosis seemed to be further supported by the presence of a thyroid adenoma. Those authors observed that the B.M.R. may be significantly raised in hyperadrenalism.

Espersen and Dahl-Iversen (1946) describe another case in which a diagnosis of thyrotoxicosis led to treatment with methyl thiouracil. This was followed by improvement, but was discontinued because of toxic manifestations. Subsequent thyroidectomy led to a recession of symptoms for five months, when further attacks of hyperadrenalism suggested the correct diagnosis of phaeochromocytoma, which was successfully treated by adrenalectomy.

In view of the similarity of the two syndromes it is surprising that this diagnostic pitfall has not been more widely published. Clinically the two conditions share many features. Of the symptoms [*sic*] of phaeochromocytoma Hartman and Brownell (1949) include "palpitations, hypertension, headache, nausea, pallor, perspiration, agitation, anxiety, tremulousness, dizziness, dyspnoea, pain (precordial or epigastric, or of the extremities), vomiting, glycosuria, and sometimes prostration." In the case here reported there was considerable weight loss but no loss of appetite.

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Reviews

MANCHESTER ROYAL INFIRMARY

Portrait of a Hospital. By William Brockbank. (Pp. 218, with 56 illustrations. £1 5s.) London: William Heinemann. 1952.

This is the story of the Royal Infirmary, Manchester, written to commemorate its bicentenary. The author states in his preface: "In an endeavour to make the book interesting and readable it has been thought fit to avoid mentioning unnecessarily the names of persons who have played their part in the development of the hospital." Alumni of the M.R.I. may, however, share Osler's feelings about attachment to their Alma Mater, and think that "they love her most of all for the honourable line of scientific men whose names add lustre to her Annals."

Of the few members of the staff mentioned, one of the first was also one of the greatest—Charles White, surgeon and accoucheur, who was a pupil of William Hunter, and was elected a Fellow of the Royal Society in 1762. Manchester was to wait until 1947, nigh on 200 years, before another of her surgeons, Geoffrey Jefferson, achieved this distinction.

In spite of the fact that we read of the cost of leeches, but do not find any reference to *the* Leeches, the author has succeeded in telling the story of the hospital so attractively and with such skill that he makes the dead stones live. The changing scene is shown before the background of the development of a great Cathedral and University City from a township of 20,000—with no Parliamentary representation, but with good fishing in its rivers. And yet even in 1752 Manchester had possessed a Collegiate Church for over 300 years and a famous Grammar School for over two hundred.

An adapted house in which the Infirmary was started was immediately found to be inadequate, and a new building was opened in Piccadilly in 1755. No sooner was this built, however, than extensions were required. "L'Hôtel Dieu" is indeed never completed. The buildings grew until they could grow no more in the heart of the city, and after 150 years the Infirmary was moved to an open site two miles out.

What is perhaps most striking in the Infirmary's history is that the trustees assumed responsibility for so many public services. They developed a lunatic hospital on the Infirmary site, which was removed to Cheadle in 1850 and is now the well-known "Cheadle Royal." For about 70 years they maintained public baths—cold, warm, and vapour, as well as therapeutic. For 100 years they provided for infectious fevers, first in the Infirmary precincts, and later in a separate hospital—Monsall Fever Hospital, which in 1895 was taken over by the Corporation. They developed a service for the treatment of patients in their own homes. They undertook protective inoculation against smallpox, and later instituted a vaccination service. A group of trustees formed themselves into a Board of Health and took a leading part in securing protection against the dangers of factory machinery.

One department, however, was not regarded as adequate, and in 1790 Charles White, with three colleagues on the staff, secured a house for a maternity hospital. From this small beginning there developed the famous St. Mary's Hospitals, which after many years became closely associated with the M.R.I.

By the time of the centenary big schemes of extension were put in hand, and great encouragement was given by Queen Victoria and the Prince Consort visiting the Infirmary. The enlarged building (with its domed tower and clock, and its porticos north, south, and west) was much the same as that with which the older alumni of the M.R.I. are so familiar.

Early in the history of the Infirmary clinical teaching was begun, and in the early 1800's there were two medical schools in the town.

Elections to the staff in the old days were terrific affairs entailing much canvassing, for every trustee had a vote. As many as 900 assembled on an election day. In 1872, however, an election committee of thirty was appointed, with four medical advisers. This was soon after the amalgamation of the Pine Street Medical School with Owens College, and from this time onwards the powerful and helpful influence of Owens College, later Manchester University, becomes increasingly noticeable.

The idea of moving the Infirmary from the centre of the city was first mooted in 1875. The proposal was supported by the medical committee, but in those days two miles seemed a long journey for the sick and injured, and so the scheme was rejected. The citizens had great argument for 27 years, and the decision to move was not taken until 1902, the year of the 150th anniversary of the hospital's foundation. The move was greatly facilitated by the Corporation buying the Piccadilly site and Owens College presenting the new site in Stanley Grove. A central branch was retained for 35 years, although many thought it unnecessary.

So farewell to the old, and hail to the new M.R.I.! Those who worked in the old Infirmary will find in Chapter XIV a description of the building by E. D. Telford, which awakens many happy memories—especially of the residents' common room, always known as the "Corner Room."

In the new Infirmary the author leads us to observe the growth of specialization, and records one development after another, in many of which Manchester led the way.

During the war, when the Infirmary suffered serious damage, many bold plans were made. But others besides the Board of the M.R.I. were busy planning, and eventually, on the "Appointed Day" (the fateful July 5, 1948), the M.R.I. was nationalized and became the parent hospital of the University Medical School. Cheadle Royal, however, remained outside the National Health Service after being part of the M.R.I. for 184 years.

The M.R.I. has a great history, which should be a stimulus to future generations, who, together with the present generation, owe a great debt to the author for composing this vivid picture of the past, for in the continual remembrance of a glorious past we find our noblest inspirations.

WEBB-JOHNSON.

OBSERVATION OF THE PATIENT

The Neuroses: Diagnosis and Management of Functional Disorders and Minor Psychoses. By Walter C. Alvarez, M.D. (Pp. 667. £2 10s.) Philadelphia and London: W. B. Saunders Company. 1951.

There are some kinds of clinical maturity that can come only with age and experience. This applies particularly in the human aspects of medicine and the management of the patient who has—or has not—the disease. The physician of retiring age may thus have a great deal to pass on to the next generation if he has not given way to generalizing, taken to glorifying the past, or acquired fixed frames of reference which limit his originality. Dr. Alvarez, who is emeritus professor of medicine at the Mayo Foundation, has none of these faults and has tackled with almost youthful enthusiasm and vigour the task of placing on record a lifetime of sympathetic observation. He is determined that this generation shall profit from the mistakes of the last, his own errors included.

The title is a little misleading. The book is not so much a textbook of abnormal psychology as of the psychological aspects of medical practice and of psychosomatic relations as seen by the general physician. The main thesis is that physicians and surgeons have an obligation to look beyond the area of their specialty and to take the trouble to discover why the patient presents himself with a particular set of

symptoms, and what outside events are likely to affect the outcome. It is within his province to be kindly as well as technically efficient and to treat minor neuroses as opportunity presents. Dr. Alvarez is anxious to emphasize how great are the opportunities of helping the patient in the setting of medical consultation and how barren is the doctrine that, if the disorder cannot be cut out or drugged away, it cannot be there. In giving the indications for the intervention of a psychiatrist he says, "It may be difficult to find a good psychiatrist," and does not give psychological medicine much credit for its progress in the last generation. His comments on the results of psychotherapy are especially realistic and pungent. Psychiatrists may argue in reply that his treatment of the subject is superficial, and perhaps both will be right.

This book is not designed to be read as a textbook but is ideal for reference and dipping, and in spite of its considerable bulk it is easy to read. The style is colloquial and often racy, but there is a pleasing absence of technical, and particularly of psychiatric, jargon. The use of "loved one" for a patient's relative will require amendment in the light of recent work. It might be prescribed as a non-irritating bedside book for the physician or the practitioner who, if he takes it regularly, will always have something worth while to think about when he puts out the light. Printing, paper, bibliography, and index are first class. At 50s. it is not to be bought lightly, but it may be worth adding a little to the dollar deficit to import some of Dr. Alvarez's wisdom.

ALEXANDER KENNEDY.

ART AND PERFORMANCE

Royal Northern Operative Surgery. By the Surgical Staff of the Royal Northern Hospital. Second edition. Edited by Sir Lancelot Barrington-Ward. (Pp. 638; 498 illustrations (some coloured). £4 10s.) London: H. K. Lewis. 1951.

Surgery of the Stomach and Duodenum. By Claude E. Welch, M.D. Illustrated by Muriel McLatchie Miller. (Pp. 349; 79 plates. $8.50. £3 5s. per volume if purchased separately; £3 per volume to subscribers to series of six volumes.) Chicago: The Year Book Publishers, Inc. London: The Interscience Publishers. 1951.

Surgical Technique. By Stephen Power, M.S., F.R.C.S. (Pp. 380; 198 figures. £1 10s.) London: William Heinemann Medical Books. 1951.

Despite tremendous efforts at scientific stereotyping, there is still, and is likely to be for a long time yet, a good deal of art and handicraft in the practice of surgery. For this reason there is probably no subject in which a greater difference is to be noted between textbook description (or illustration) and actual performance. So great is this difference that often an onlooker may fail to recognize that written or drawn instructions refer to a manœuvre he himself performs in the theatre. Art and handicraft can never be taught adequately from textbooks; the skilled violinist or painter does not acquire his technique by reading about it.

The proper conduct of a complicated surgical operation demands in the operator a combination of a greater variety of qualities than most other occupations—not only dexterity, artistry, and judgment, but the ability to grasp quickly the needs of the case, to improvise methods of overcoming difficulties, and, in the face of the unexpected, to devise on the spot novel yet safe means of handling the situation. All this has to be done under the strain of appreciating the hazard to the patient and within a certain time limit. It is small wonder that to the initiated there is no more inspiring sight than to watch a master surgeon perform a difficult operation. Small wonder too that this cannot be learnt from textbooks; yet such guides have their uses and the surgeon must to some extent be dependent on them.

Books on operative surgery can be divided roughly into two categories. The one attempts to pass on to the reader some of the practical experience and judgment of the author; the other treats the subject more theoretically, with description of the procedures as they might be carried out on a perfect theoretical body. The books at present under review illustrate this point.

In the *Royal Northern Operative Surgery*, written by the various members of the hospital staff, we have a real practical guide in which the authors make no attempt to cover the whole field but tell us of the methods they have themselves successfully used in a very wide range of surgical conditions. It is indeed surprising how much has been included within the compass of some 600 pages, for not only are adequate chapters on thoracic and neurosurgery to be found, but there is even room for a short one on the commoner gynaecological operations. There are ample illustrations, many of them actual photographs of cases. This book will be instructive to the ordinary surgeon, especially to the diminishing number whose work can be said to be truly general.

In *Surgery of the Stomach and Duodenum* we have an example of the second type of book. Here are a large number of well-executed, clear line-drawings with accompanying brief letterpress. Almost every operation upon the stomach performed nowadays is illustrated, even including a phrenic crush when treating hiatus hernia. The space devoted to the transthoracic approach in the larger gastric resections suggests that this operation is becoming as popular in the U.S.A. as it is in this country. This is essentially a book for the examination candidate to peruse. The claim of the publishers that it sets a new standard of clarity is substantiated. If any criticism is offered it is that the drawings are deceptively clear and may give the unwary a false idea of ease of accomplishment.

On quite different lines Mr. Stephen Power has written a small book on *Surgical Technique*. This is on those detailed points in operative technique which often make all the difference to the outcome of an operation or to the facility with which it is performed. Although some of the points are comparatively elementary, the practical surgeon will find in these pages interesting reading. I particularly liked one quotation from Thomas Keith, 1873: "For my own part, when a case goes wrong after operation, I have seldom to look far beyond myself for the cause of failure—something done, something not done. This is a lesson hard to learn; we blame persons, things, accidents and circumstances rather than ourselves." Would that one could always remember this.

NORMAN C. LAKE.

FREUD ON DREAMS

On Dreams. By Sigmund Freud. Entirely new translation by James Strachey. International Psycho-Analytical Library No. 42. (Pp. 80. 9s. 6d.) London: The Hogarth Press and the Institute of Psycho-Analysis. 1952.

In the days when only a few translations from his works were available, English readers frequently made their first acquaintance with Freud by tackling his *Interpretation of Dreams* (1900), an approach which more often than not ended in a considerable damping of their ardour. Freud was clearly aware of the need for a simpler exposition, and in 1901 published this monograph *On Dreams*, which was in effect a résumé of his earlier monumental work. It gives in brief outline an account of the processes of dream formation and of the way in which the latent content of dreams can be uncovered by psycho-analytic techniques. Although the presentation is extremely simple, the reader cannot be spared a certain amount of technical detail, the assimilation of which, however, is rendered easier by appropriate quotations from a number of actual dream analyses.

This is essentially a book for the psycho-analytical beginner and for those general readers, both psychiatric and lay, who wish to inform themselves about the function of the unconscious mind. If regarded as an introductory brochure, one comment is permissible. Some of the space at present devoted to rather pedantic editorial glosses might well have been given to more copious annotations on those points of theory which Freud modified in his later works. This omission should be rectified in future editions

EDWARD GLOVER.

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THE PRESIDENTIAL ADDRESS

Dublin medical men have made fundamental contributions to the study of diseases of the heart. It is a happy chance, therefore, that a cardiologist has been chosen to preside over the Joint Meeting of the Irish Medical Association and the British Medical Association in Dublin this year. In his Presidential Address on Monday this week, which is published in our opening pages, Dr. P. T. O'Farrell took a brief but penetrating glance at some of the topics, medical and medico-political, at present to the fore in the minds of the profession on both sides of the Irish Sea. In the more leisurely atmosphere of Dublin, over which there still lingers the seductive charm of the age of reason, Dr. O'Farrell, if one may read between the lines, does not find that distance lends enchantment to the medico-political view of Britain. There is a pleasantly detached urbanity in his observation on the concept of the Welfare State: "This doctrine is, of course, not entirely unobjectionable." He sees in this concept the dangers of "an exclusive or excessive responsibility of the State over the liberty of the individual and the family way of life," and a possible loss of independence and individual incentive in a community that is too much governed. Nevertheless, Dr. O'Farrell freely admits that social medicine has "conferred inestimable benefits on the community and that still more can be done to extend the scope of its activities." He would like to see the medical profession take a leading part in this crusade, and wisely sees a successful outcome only in harmonious and continuous partnership between Governments, the medical and allied professions, and responsible leaders of the community. This is indeed the problem before the profession not only in Eire and Britain but in all other civilized countries, and it is good to see a man occupying the distinguished position Dr. O'Farrell holds so fully alive to the new ways of thinking and to the pitfalls that surround them.

Anyone who to-day discusses the general themes of medicine finds himself inevitably confronted with the position and problems of general practice and the general practitioner. The Danckwerts award has in Britain gone a long way to meet one of the justifiable discontents of this most hard-working section of the medical community, and the general acceptance of the award by Parliament, Press, and people is a welcome acknowledgment that the labourer is worthy of his hire. But the discontents among general practitioners go deeper than this, and it is to some of these that Dr. O'Farrell aptly addresses himself. The profession, he says, has been at fault for many of the things that have gone wrong, and he tilts sharply at the trend towards specialization, "which has been encouraged to an unreasonable degree." He usefully reminds us that 90% of illness is made up of the common ailments—ills which can be dealt with competently only by the general practitioner, or, to use a preferable term, the family doctor. Dr. O'Farrell urges that many more students should be encouraged to aim at general practice, and he would like to see the established general practitioner taking an active part in the education of students who want to pursue this desirable if arduous career. It is interesting to see him, as others have done in recent years, urging a period of apprenticeship "in further preparation for his entry to the ranks of general practice." In continuance of his argument against specialization Dr. O'Farrell is cautious about accepting the idea of a College of General Practice, seeing in the establishment of this "the risk of grading of the general practitioner, and causing a category of specialists within its own ranks." He would, if we read him aright, prefer to see the doors of the hospitals "freely opened to the practitioner, so that he can follow the progress of his patient and test his diagnostic skill at every stage of an illness," and he hits the nail on the head in his observations of the bad effects of overwork. "Overwork and good medicine are mutually antagonistic." The doctor who has to fill too many forms and see too many patients is driven to shed his load by referring "some of his patients with undue precipitancy to a specialist or a hospital. The sharing of liabilities in this way often leads to delay in starting treatment, and personal touch with the patient may easily be lost."

What the new President has to say about general practice will find a ready response in the minds of his readers. Leisure seems to have gone out of the professional life of Britain, and to-day more than ever the medical man, whether a general practitioner or not, needs leisure to keep up with the breathtaking advances of medical science. Compared with his predecessor of as short a time ago as a quarter of a century, the general practitioner of to-day has a new knowledge to acquire, and it is perhaps this as much as anything else that causes disquiet among those thousands of G.P.s who have to fight against the clock

in their daily work. These many problems cannot all be solved at once, but they must be solved without, in Dr. O'Farrell's words, " the imposition of bureaucratic State control."

The B.M.A. has met six times in Ireland—in Dublin, Belfast, and Cork—and this is the fourth time Dublin has acted as our generous host. The President reminds us in his Address that it was at the Dublin meeting of 1867 that the scientific sessions of the B.M.A. began, when Lister gave his address " On the Antiseptic Principle of the Practice of Surgery." It must have been the intellectual challenge that Dublin has always offered both to itself and to its visitors that was responsible for two new departures in the scientific part of the meeting this year. The first is the holding of plenary scientific sessions, and the second the setting up of a scientific exhibition. Those who have had the opportunity of seeing the scientific exhibitions at the annual meetings of the American Medical Association have come away impressed not only by their excellence but by their high educational value. It will probably be many years before we shall reach the standard of excellence of the A.M.A., if for no other reason than the shortage of money. But a start has been made. Now that the advances in medical science come principally from the team-work of many specialists the need grows for a synthesis of knowledge through the symposium and the plenary session. This, too, has been started in Dublin this year. It is surely no accident that it has been in Dublin that the three main features of the scientific side of the Annual Meeting have had their beginning. Dublin may well take pride in this, as we on our side of the water take pride in gathering together in that historic city and in hailing its distinguished physician, Dr. O'Farrell, as our President, whose Address was heard with such appreciation on Monday—an appreciation now to be shared by a wider audience.

HAEMORRHAGE IN LATE PREGNANCY

Strictly speaking, antepartum haemorrhage implies bleeding from premature separation of the placenta after the 28th week of pregnancy and before the end of the second stage of labour. It is subdivided according to whether the placenta is sited in the upper segment of the uterus (accidental haemorrhage) or partly or wholly in the lower segment (placenta praevia). In practice, however, the term antepartum haemorrhage is often used loosely to include all cases of vaginal bleeding after the 28th week, and all of these not proved to result from placenta praevia are designated accidental haemorrhage. The consequence is that many unrelated conditions may be grouped together. Certainly bleeding which is not coming from within the uterus but arises, for instance, in a cervical lesion should be excluded, but in many reports from maternity hospitals in this country this is not done. Even when the haemorrhage is seen to come from within the uterus its cause and even its source may remain obscure, as Browne has long emphasized.[1] It most often originates from the placental site, but not invariably so, for the bleeding may be not maternal but foetal. The chief source of such haemorrhage is vasa praevia, a condition with a foetal mortality in reported cases of over 50%. Rupture of vasa praevia is a small but definite risk attached to artificial rupture of the membranes, especially when the placenta is low-lying, but vasa praevia may also occur even when the placental site is high in the upper segment. Further, Torrey[2] has pointed out that, while the condition is usually one of vasa praevia in the strict anatomical sense, sometimes the umbilical vessels do not cross the internal os and the point of rupture is not adjacent to the edge of the placenta. Torrey prefers the term " ablation of the umbilical vessels " for the latter group, but in both a prerequisite is velamentous insertion of the cord, an anomaly which occurs much more commonly in twin pregnancies and is almost the rule with triplets. The clinical diagnosis of rupture of the umbilical vessels, although of vital importance to the foetus, is a matter of great difficulty. A possible aid to diagnosis, first suggested by Williamson[3] in 1912, is to take a smear of the blood draining from the vagina and examine it for foetal blood elements such as nucleated red cells, the presence of which would be an indication for immediate delivery.

Even when the condition of vasa praevia can be excluded there may remain difficulty in distinguishing between unavoidable and accidental haemorrhage. Major degrees of placenta praevia create no difficulty, but minor degrees if unproved, as commonly happens, are tabulated under accidental haemorrhage. There is a further difficulty. When placenta praevia exists the bleeding is usually ascribed to the taking up of the lower segment, but there is no reason why the mechanism may not sometimes be the same as in premature separation of a placenta in the upper segment. Thus the bleeding in placenta praevia may not be always due to the same cause, and it may be

[1] *Antenatal and Postnatal Care*, 1946, p. 236, London.
[2] *Amer. J. Obstet. Gynec.*, 1952, **63**, 146.
[3] *J. Obstet. Gynaec. Brit. Emp.*, 1912, **21**, 203.
[4] Weiner, A. E., *et al.*, *Amer. J. Obstet. Gynec.*, 1950, **60**, 379.
[5] Page, E. W., *et al.*, ibid., 1951, **61**, 1116.
[6] Ibid., 1950, **59**, 13.
[7] Ibid., 1951, **61**, 20.
[8] *Proc. roy. Soc. Med.*, 1951, **44**, 489.

that the different mechanisms have different importance, especially in so far as foetal prognosis is concerned.

Accidental haemorrhage proper, or abruptio placentae as De Lee called it, is traditionally associated with the toxaemias of pregnancy, although the exact mechanism of separation is still debated. It is disconcerting, however, to find that the proportion of cases of accidental haemorrhage in which toxaemia has been present has varied from over 80% to under 30% in different reported series. This variation probably reflects differing criteria for the diagnosis of toxaemia, but the lower figure is more likely to be accurate if all cases are taken into account, and the higher if only the more severe types, including the concealed variety, are considered. But there still remain many cases of antepartum haemorrhage not due to placenta praevia or toxaemia. A few are caused by direct trauma, with the obstetrician most often the agent and external version with or without anaesthesia most commonly the occasion. It has recently been suggested that premature separation of the placenta may be due to defects in the mechanism of blood coagulation, notably afibrinogenaemia,[4] but there is reason to believe that such defects are less likely to be cause than effect.[5] Sexton and his colleagues[6] believe that the frequent association of abnormalities of placental development with haemorrhage has not received enough attention. They consider it significant that the placenta was circumvallate in 82 of their 276 cases of non-toxic premature separation of the normally situated placenta, and they suggest that in these cases separation may be initiated by senile degenerative changes at the extrachorionic margin of the placenta. In another 32 of their cases the bleeding was ascribed to rupture of the marginal sinus, which in the opinion of Fish[7] is liable to be torn because of its location and membranous structure. Clinically rupture of the marginal sinus simulates placenta praevia in that the haemorrhage is painless and the blood bright red. The chief difference is that in placenta praevia bleeding most often begins before labour, whereas marginal sinus rupture does not as a rule cause bleeding until labour is in progress. The diagnosis is made by studying the placenta after delivery and finding old or recent clot adhering to a portion of the placental margin, overlying a tear in the marginal sinus and spreading out over the adjacent membrane. There is, however, a surprising disparity between the two sets of figures. Sexton found the incidence to be less than 7% in 476 cases of premature separation of a normally situated placenta, while Fish ascribed the bleeding to marginal sinus rupture in 33% of 147 cases of antepartum haemorrhage including placenta praevia, and he reported the much lower foetal mortality rate of 4%. To complicate matters still further, Hamilton and Boyd,[8] after studying 21 placentas *in situ* in late pregnancy, have reported that they cannot find any macroscopical or microscopical evidence of the existence of a marginal sinus.

With antepartum haemorrhage remaining unexplained in not less than 20% of cases, there is an obvious and urgent need for further research.

THE SUPPLEMENTARY ESTIMATE

Publication of the Supplementary Estimate to give effect to the Danckwerts award means that only one more seal is needed before the money is made available—ratification by Parliament. The additional gross money required is about £40m., from which superannuation contributions have to be deducted. Whether the Opposition will choose a Supply day to debate the Supplementary Estimate is at present unknown. The Government's memorandum issued with it proposes that in future the central pool shall be distributed "on the basis of the arrangements" described in the report by the Working Party on the distribution of general practitioners' remuneration.[1] It also states that the arrears will be distributed in accordance with existing arrangements, since this is the only practicable method; this was the procedure advocated by the General Medical Services Committee and endorsed by the Special Conference of Local Medical Committees on June 26.

The Labour Party has already announced that it will not oppose the Danckwerts findings.[2] Indeed, it could hardly do otherwise, for when in power it accepted the Spens report, which has all along been, and continues to be, the agreed basis of general practitioners' remuneration in the N.H.S. It agreed last year that the proper interpretation of the report should be submitted to adjudication, but in its statement already referred to and through its spokesman and former Minister of Health, Mr. Hilary Marquand,[3] it has cavilled at the Working Party's agreement for distributing the money in future. The criticisms are of two kinds. The first is that the scheme does not give enough help to the young and poorer-paid doctors. There are doctors also, and not only among the young and poorer paid, who have given expression to similar doubts. Trial of the scheme will show whether the doubts are justified, but it may be said now that they are not shared by the Assistants and Young Practitioners Subcommittee, whose members are familiar with this problem, both from their own experience and from the representations made to them by the young doctors whom they represent. In addition, the Special Conference endorsed a policy of removing any defects in the scheme that experience of

[1] *Supplement*, June 7, p. 283.
[2] *British Medical Journal*, July 5, p. 30.
[3] *The Times*, July 3.
[4] *Supplement*, July 5, p. 4.

its working may reveal. If certain groups of doctors who are expected to benefit do not do so, it will be "left to the Working Party provisionally to allocate an appropriate proportion of the final settlement money for the purpose of remedying any obvious defects in the distribution scheme."[4]

The second criticism is that the scheme does not give promise of a better service to the public. There is nothing much wrong with the present service. If it has deteriorated since 1948 those who introduced the Health Service in the form they did are themselves to blame. But what the Working Party had to devise was a scheme "to enable the best possible medical service to be available to the public, and to safeguard the standard of medical service by discouraging unduly large lists." The Working Party's recommendations go a long way to fulfil these aims. Those who believe that partnerships afford most doctors the best opportunities for sound general practice have had their contention met in the Working Party's report, for one of its principal arrangements will encourage the establishment of more practices of this type. The loading of the capitation fee for patients in the 501–1,500 range should discourage "unduly large lists"; what is more significant is the restriction for the single-handed principal to a list of 3,500. While this may be desirable—and has been accepted—it does limit freedom of choice. It has been contended that it is difficult for the young man to enter general practice; the new scheme should make things much easier. Finally, the financial burden that many doctors have borne through four years of serious underpayment is at last removed, and with it should go that consequent discontent which is bound to impair the harmonious working of any service.

THE RIGHT GAS

Mistakes in identifying gas cylinders have happened so often, and sometimes with fatal results, that all who use them will welcome any attempt to discriminate between cylinders unmistakably. Discussions between various interested organizations have at last resulted in "a high measure of international agreement" on the colours to be used in future to signify the contents of each cylinder. The secretary of the Medical Defence Union describes at page 92 how the changes are to be carried out, and emphasizes the possible dangers from confusion during the transition stage. Nitrous oxide cylinders are the first to be repainted—in French blue (a rich blue) instead of black. The Ministry of Health has sent instructions to hospitals on how the cylinders are to be recalled for painting, August 1 being the date when this begins. Changing the cylinder colours for all medical gases is expected to take about 12 months, and the need for all doctors and nurses to be on the alert for at least the next 18 months is clear. But what is also apparent from a perusal of cases that have come before the courts is the enduring need to pay special attention to identifying the contents of a cylinder, for in the heat of the moment the coat of paint can be overlooked, with fatal results. Last year, for example, the case was reported[1] of six people in succession who handled a cylinder believing it to contain oxygen; only the last correctly identified the contents as carbon dioxide, though the cylinder was painted green, and all knew the meaning of the colouring. But at least international agreement on the colours will help doctors who come here from abroad to identify the gases readily: fatalities have occurred from their making mistakes in the past, especially during the last war. The measure likely to ensure greatest safety is to fit non-interchangeable valves so that anaesthetic apparatus cannot be connected up wrongly, but, according to the secretary of the M.D.U., "this awaits further conferences and agreements." We may hope that his organization and the others concerned will continue their useful work and reach agreement as soon as possible.

1 *British Medical Journal*, 1951, 1, 1455.

CORNEAL GRAFTING ACT

The Corneal Grafting Act,[1] 1952, received the Royal Assent on June 26 and will come into operation at the end of September, by which time centres for the collection of eyes will be set up in several parts of the country. The Act enables eyes to be removed from dead bodies in two differing sets of circumstances. In the first place, when a person has expressed a request that his eyes be used for therapeutic purposes after his death "the party lawfully in possession of his body . . . may, unless he has reason to believe that the request was subsequently withdrawn, authorize the removal of the eyes from the body for use for those purposes." Secondly, "the party lawfully in possession of the body of a deceased person" (including, of course, hospitals) may authorize eyes to be removed from a body provided that during life the patient had expressed no objection to this and that his or her relatives were not against it. In a statement about the Act the Ministry of Health advises those who wish to offer their eyes for use after death to make a written statement of their wish and give this to their family or anyone else with whom they live. They should also give a copy of the statement to the executors appointed to carry out their will, and if they enter a hospital for treatment they should let the hospital know of their wish. The Ministry's statement makes it clear that there is no danger that anyone who does not wish his eyes to be used will have them removed after death.

The growing importance of corneal grafting as a method of preventing blindness and the need for more donor material were discussed in these columns last year,[2] and the sponsors of the Corneal Grafting Act, including Mr. Gerald Williams, M.P. for Tonbridge, who introduced it in Parliament, are to be congratulated on the successful outcome of their work. It should now be possible for the hospitals at which corneal grafting operations are undertaken to obtain all the material they

1 Corneal Grafting Act, 1952, 15 & 16 Geo. 6 and 1 Eliz. 2, Ch. 28. Obtainable from H.M.S.O., London, price 2d.
2 *British Medical Journal*, 1951, 1, 575.

need. Probably enough eyes will be obtained through centres organized near these hospitals for it to be unnecessary to spread the collecting net widely over the country. On the other hand, all offers from in-patients who later die in hospital or from the relatives of those who die at home should be accepted, if possible, and the Ministry will soon be sending technical advice to hospitals about this. Family doctors will probably receive inquiries from patients and their relatives, and in areas covered by a collecting centre there should be little difficulty in meeting a request that a person's eyes should be used after death for corneal grafting. It used to be thought that eyes should be removed within two hours of death, but this time has now been extended and grafting has been successful with eyes removed up to ten hours after death. Vision has been restored by grafts from eyes which have been stored for as long as ten days.

CELEBRATIONS AT MANCHESTER

"Manchester Royal Infirmary is one of the great hospitals of Europe and an expression of the genius of Lancashire," wrote Sir Geoffrey Jefferson. On p. 88 of this issue Dr. William Brockbank sketches the infirmary's history since it opened its doors 200 years ago this July 27, and shows how rapidly it grew. In 1766 was added a lunatic asylum where persons disordered in their senses would find "that humane treatment and judicious advice that they had no encouragement to expect in private madhouses." As long ago as 1867 a convalescent home was started at Cheadle, and a separate fever hospital a few years later. The hospital was a leader in the provision of public baths and a public health service, and in the prevention of accidents in factories. Its medical school has produced many eminent men, and three former Manchester students, Lord Moran, Lord Webb-Johnson, and Sir William Fletcher Shaw, were recently presidents simultaneously of the three Royal Colleges.

Manchester has many claims to be the capital of the northern half of England. It is a great industrial city and, through its Ship Canal, a great port. It maintains an internationally read newspaper (the *Manchester Guardian*) and a world-famous orchestra (the Hallé) Its Grammar School and University are outstanding among Britain's educational institutions. The scientific tradition there dates from the mid-eighteenth century when the Manchester Literary and Philosophical Society was founded with such members as Benjamin Franklin, Erasmus Darwin, and Josiah Wedgwood, and later with men like Thomas Henry, who enunciated the law of partial pressure of gases, and John Dalton, the colour-blind author of the modern atomic theory. It was to the Society that J. P. Joule first communicated his discovery of the mechanical equivalent of heat, an important basis of modern thermodynamics. To-day this scientific tradition has flowered in medicine as well as in physics—in neuroanatomy and neurosurgery, renal pathology, and diseases of the blood.

Manchester is a vast city, reaching out across the frontiers of local government to touch Liverpool. Its greatness to-day is based on more than textiles, and there is talk of founding a great new technical university there. Manchester Royal Infirmary, which is now celebrating its bicentenary, has a great future before it.

NEWS OF PHYSICAL MEDICINE

Physical medicine had its beginnings as a therapeutic specialty in the guidance of physiotherapy. It now embraces, however, the fields of diagnosis and treatment of medical disorders of the locomotor system, the application of physical methods in these and other disorders, and the comparatively new fields of prevention of incapacity and medical rehabilitation. This evolution has been accompanied by a remarkable swing away from merely passive, palliative, and often ineffectual treatment to a dynamic programme of activity in which the patient's own efforts to restore his health are regarded as the first and most important step in recovery. This was well illustrated by the work carried out in the physical development centres of the Army and the medical rehabilitation centres of the Royal Air Force in the last war. Such an attitude of activity is reflected in many of the papers to be read at the International Congress of Physical Medicine at King's College, London, between July 14 and 19. Advances in the treatment of acute diseases in recent years have drawn attention to the necessity for further study of chronic disease, particularly rheumatic disorders, and it is natural that one of the scientific sessions of the Congress should be devoted to these illnesses, where medicine has to look to physical methods for symptomatic relief, restoration of function, and a means of enabling the patient "to make do with what is left." The adjuncts to diagnosis which physics affords have made remarkable advances, particularly in the use of electrical methods. No fewer than five papers on electrodiagnosis are being read, and these are mostly directed to the new and important technique of electromyography, which is being watched with interest by physiologists and neurologists as well as by physical medicine specialists. Physical medicine as a specialty has much to offer the older sciences, and we wish this International Congress every success in its deliberations.

BRITISH EMPIRE CANCER CAMPAIGN

The twenty-ninth report of the British Empire Cancer Campaign, whose annual meeting is referred to on another page, is possibly of more than usual interest in view of criticisms which are being levelled at cancer research in general both by the public and in the medical press. It is suggested on the one hand that there is not enough research going on, or alternatively that it is not being directed along the most profitable lines. The 350 pages of this year's report follow much the same pattern as those of previous years, and to the ordinary doctor reading them there seems to be a good

deal more about carcinogenesis than about any advances in the treatment of cancer. But as Lord Horder and Sir Heneage Ogilvie say in the introduction, "Stone by stone the wall is growing." It is only by systematic study such as is described in this report that progress can be made, though the ordinary medical reader cannot help feeling that the dimensions of the wall are likely to be colossal before the final stone is laid.

The results of treatment in certain sites continue to show steady improvement. Surgery, not necessarily more bold than in the past but rendered less hazardous by modern methods, and radiotherapy applied by machines of increasing power and complexity, together hold out more hope for the sufferer, sometimes of cure, often of considerable palliation. Knowledge of the uses and effects of isotopes is still comparatively meagre, but naturally continues to engage the enthusiasm of many workers. On theoretical grounds chemical research should offer the greatest promise of success in the treatment of cancer through chemotherapy. It is not surprising, therefore, that biochemical work figures prominently in the report.

The volume, though bulky, contains after all only the barest outline of the vast amount of work which has been done during the year, and it is neither profitable nor proper to select particular subjects for comment. To the practising doctor those that deal with clinical research probably appeal most. Those who treat patients at cancer centres will take particular note of the report of an investigation (if they observe it, for it occupies but a few lines) designed to ascertain why patients delay in seeking advice when suffering from cancer. For at the moment it is still true to say that the only hope of suppressing the disease lies in early treatment. Cancer may be "early" from the pathological aspect, and this is largely a matter of luck, or it may be "early" in respect of the length of history, and this is a matter for the patient and his medical adviser. The latter has been under fire for some time: it is now proposed to test upon the former the effect of propaganda in an area where complete registration and follow-up have already been arranged.

HORMONES AND PERSONALITY

The interest of psychiatrists has been turned many times, usually with all too little in the way of positive results, to the endocrinological aspects of personality and the influence of disturbances in endocrine balance on mental disorder. In recent work the suprarenal has come to occupy a place of importance hardly less than that earlier taken by the thyroid and the pituitary. Interest is revived in the report[1] of Broster and Allen describing the relief of paranoid psychoses accompanying virilism in female patients by the removal of an adrenal tumour. A considerable amount of work is now being done with A.C.T.H. and cortisone in such conditions as delirium tremens and states of exhaustion. Furthermore, cortisone, when used for the treatment of rheumatism, has been found to produce euphoria and even states of excitement. According to a verbal report he gave when on a visit to this country, Hoagland has performed double adrenalectomy on chronic schizophrenic patients, who are being kept alive by cortisone and desoxycorticosterone.

Elsewhere in this issue workers at St. Bartholomew's and St. Ebba's Hospitals describe two experiments they have made on the treatment of schizophrenic and psychopathic patients with another adrenal cortical substance, dehydro*iso*androsterone. The results they obtained are certainly interesting. As might have been expected, the schizophrenic group derived less benefit than the psychopaths. Nevertheless a definite change in the pattern of behaviour was shown. Although these patients were selected on a combination of physical immaturity with low or abnormal ketosteroid excretion, and they mainly showed an anergic, solitary, apathetic clinical picture, the degree of improvement obtained does not seem to bear any close relation either to the degree of abnormality in ketosteroid excretion before treatment or to the extent to which it was corrected. The improvement, although in two cases it was gratifying, is not conspicuous. It resembles in degree the improvement obtained in the past when psychological treatment, or energetic work therapy, was begun with patients in chronic wards who had not received much attention. Cardinal and positive symptoms appear to be little altered; the main benefit was shown in the relief of lack of confidence and apathy and, unless the patient was made excited and obstreperous, improvement in social attitude. It does not seem likely that this treatment goes to the heart of the matter and opposes the schizophrenic pathogenic process itself. But further experiment is certainly justified, especially with a view to delineating the type of patient most likely to benefit from this and similar methods of treatment. An excessive optimism would not, however, be warranted.

In the psychopathic group the results obtained are more encouraging, as they were more consistent. All these patients were mere lads, and the ones who responded to treatment showed a pattern of physical immaturity, even effeminacy, timidity, social inadequacy, and lack of drive. More mature individuals, of an aggressive rather than an inadequate type, were only made worse. The effect of treatment, which was continued only over a few months, was to reduce the inadequacies which had been the grounds of selection.

This clinical group is clearly a more promising one than the schizophrenic group for the prosecution of further experiments in treatment. The therapist has not, as with psychotic patients, to cope with the results of a morbid disintegration of the personality, but only with a personality which has failed to mature and which shows certain deficiencies. These deficiencies are themselves of a type to be explicable on an endocrine basis, even if ketosteroid estimations do not prove to be especially relevant. Perhaps the most noteworthy feature in the results was the alteration of homosexual into heterosexual tendencies. The authors are probably right that administration of androsterone will probably have to be continued for a longer period than they allowed for lasting results to be obtained.

[1] *British Medical Journal*, 1945, 1, 696.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

LACERATIONS OF THE HAND

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Many lacerations of the hand require to be treated in hospital, and those who work outside the hospital service may feel that they have little to do with the treatment of these injuries. It is, however, the general practitioner or the industrial medical officer who is first consulted, and it is he who must decide which patients may safely remain under his care and which require more specialized treatment. This is no light responsibility, for upon his judgment may depend the future livelihood of the patient. The hand does not readily forgive errors in treatment. Skin loss which is allowed to heal slowly by granulations instead of being closed by plastic surgery will cause fibrosis and disabling skin contractures. Exposure of deep structures without the aid of modern theatre conditions may lead to severe reaction, oedema, and a stiff useless hand. Infection may complete the ruin. Fortunately it is also true that few other regions of the body are more responsive to careful and delicate work, and much can be accomplished by reconstructive surgery if the early management has been correct and rapid primary healing obtained.

Consistently good results depend upon a high standard of treatment from the time the accident occurs until the final stages of recovery, and the more each one of us knows of the general plan the better can we play our part when the need arises. If, therefore, much of the ground covered in this article is concerned with hospital care it is hoped that there may be something of interest and value for the general practitioner.

Diagnosis

A careful assessment of the hand should be made to determine the extent of the injury. Small wounds may be associated with important tendon or nerve division, and these complications may easily be overlooked unless suspected and investigated. The patient should not be the one to discover it later and inform his doctor. A diagnosis should be made by observing movements and sensation, and under no circumstances by groping about in the wound for the cut ends of tendons and nerves.

Mistakes can easily arise when assessing the significance of finger movements, owing to the complex arrangement of muscle actions.

The fingers are extended at the metacarpo-phalangeal joints by the extensor digitorum communis. Extension at the proximal and distal interphalangeal joints is by the intrinsic muscles—interossei and lumbricales—or by the extensor digitorum, depending upon the position of the metacarpo-phalangeal joint. When this joint is flexed more than 45 degrees, extension of the middle and distal phalanges is by the extensor digitorum, but when the flexion angle is less than 45 degrees, control of distal extension is taken over by the intrinsic muscles.

The interossei and lumbrical muscles are the prime flexors of the fingers at the metacarpo-phalangeal joints. The flexor digitorum sublimis flexes the proximal interphalangeal joints and the flexor digitorum profundus flexes the distal interphalangeal joints; they both also serve as weak subsidiary flexors of the metacarpo-phalangeal joints.

The interossei muscles abduct and adduct the fingers in relation to the middle finger. This movement can be simulated by the combined action of long extensor and flexor muscles, for as the fingers are extended they fan open, and as they flex the fan closes again. Interosseus function can, however, readily be determined by the fact that they are the only muscles capable of moving the middle finger from side to side in the plane of the extended fingers.

The median and ulnar nerves as they approach the wrist pass within a quarter of an inch (6 mm.) of the skin surface. The digital nerves pass down the fingers even closer to the surface. It is not surprising that nerves of the hand are often injured, even when the surface laceration is deceptively small.

The median nerve passes deep to the transverse carpal ligament into the palm and divides into a lateral and medial part. The lateral division gives a branch to the thenar muscles, supplying the abductor pollicis brevis, opponens, and the superficial head of the flexor pollicis brevis, and then proceeds to form the digital nerves providing sensation to the thumb and radial side of the index finger. The medial division forms the digital nerves to the ulnar side of the index finger, both sides of the middle finger, and the radial side of the ring finger. The lumbrical muscles to the index and middle fingers are supplied by these digital branches of the median nerve.

The ulnar nerve passes anterior to the transverse carpal ligament to divide into superficial and deep branches. The superficial, or sensory, branch forms the digital nerves to the ulnar side of the ring finger and both sides of the little finger. The deep, or motor, branch supplies the hypothenar muscles, all the interossei muscles, the lumbricals to the ring and little fingers, and those muscles of the thenar eminence not supplied by the median nerve.

Variations in the nerve supply to the intrinsic muscles are not uncommon. Sensory nerve division results in loss of superficial and deep sensation, and in dryness of the skin due to lack of autonomic function. Motor nerve function can be readily tested in the hand. The action of the interossei will determine the integrity of the ulnar nerve. The median nerve is tested by observing the abductor pollicis brevis and the opponens pollicis; the abductor raises the thumb from the plane of the hand, the nail remaining at right-angles to the palm, whereas the opponens carries the thumb round to face the fingers, the thumb-nail becoming parallel to the plane of the hand.

Principles of Treatment

Lacerations involving severe skin loss and nerve, tendon, or bone damage should receive no treatment outside hospital other than a copious protective dressing and a compression bandage to control haemorrhage. The hand and forearm should be immobilized by a simple splint. It is very rarely necessary to use a tourniquet; indeed, any tourniquet, other than a pneumatic one, applied to the upper limb is so fraught with peril that I would be most hesitant to use it. Severe lacerations are surgical emergencies of the highest order, and there should be the least possible delay between injury and full surgical treatment. Anti-tetanic serum should be given, and in all extensive lacerations a short prophylactic course of penicillin is advisable.

General anaesthesia is the most suitable whenever extensive surgery is required. It is fortunate that these patients do not usually suffer from serious shock, for the operative time may well run into two or three hours.

Brachial block analgesia or regional block is of use at times in special cases; for minor injuries of the fingers digital nerve analgesia is convenient. Infiltration around the base of a digit will give effective analgesia, but on no account must a constricting agent such as adrenaline be used with the analgesic solution. Vascular constriction may be so complete and persistent that gangrene of the digit can follow.

The hand is washed thoroughly with a detergent, such as cetrimide or soap and water, while the wound is kept covered with a gauze pack. The skin is dried and then painted with a suitable antiseptic—there is none better than iodine in 90% alcohol. The wound itself is then washed thoroughly and repeatedly with a detergent which is not harmful to the tissues. Strong antiseptics do more harm to the living tissues than the good they may do by destroying a few organisms.

All severely damaged and devitalized tissue should be excised, as in all open wounds. Non-viable and badly crushed skin must be removed, even when this involves loss of large areas of skin, but it is unnecessary to make a formal removal of a thin strip of skin in every lacerated wound of the hand. A laceration caused by a sharp implement will need little if any skin edge removal, but when a tearing or crushing element has been present quite extensive areas of skin and deeper tissues may be devitalized and require removal. This type of injury needs special care, because of the risk of infection beginning in damaged tissue.

Remember that any wound, small or large, may readily become infected, and that contamination from careless handling or breathing upon the wound need not and should not occur. A sterile technique and a face-mask are necessary for all wound dressings.

Skin Loss

It is of the utmost importance to obtain skin cover, and in the primary treatment of a laceration bone, tendon, and nerve repair must take second place to the restoration of skin loss. Raw areas and slowly healing wounds lead to prolonged tissue reaction, oedema, and fibrosis, and thus to stiffening of the hand.

Many minor lacerations may be sutured without tension and rapid primary healing obtained, but lacerations with loss of skin may leave vital structures exposed when all possible closure by suture has been completed (Fig. 1). Unless these structures are covered, infection will follow and lead to much delay before reconstructive surgery can begin.

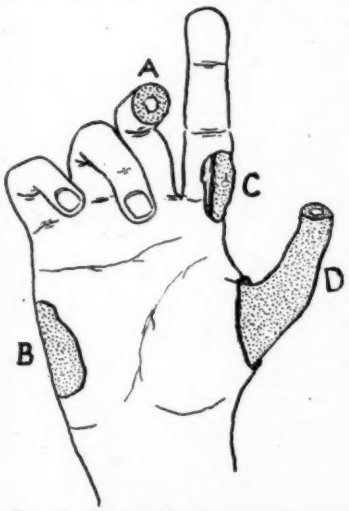


FIG. 1.—Types of skin loss showing suitable methods of repair. A, Whole-thickness free graft. B, Partial- or whole-thickness free graft. C, Tendon exposed, local flap necessary. D, Avulsion of skin, subcutaneous tissue, and terminal part of thumb, distant pedicle flap necessary.

Loss of skin may be made good by free skin grafts and by flaps, local or distant. Free grafts of either partial or full thickness will take readily upon the vascular structures of the hand, and weeks of disability can be prevented by the simple procedure of covering raw areas with skin taken, for instance, from the same forearm. The graft is stitched carefully in place and covered with wide-mesh vaselined gauze and a well-applied pressure dressing. This method is particularly suitable for traumatic amputation of the finger-tips, for, even when the phalanx is divided, the exposed medullary bone will give sufficient blood supply for survival of the graft. The greatest danger to these grafts lies in the formation of a haematoma; if haemorrhage persists after wound toilet, despite sustained pressure, a simple dry dressing may be applied and the grafting performed 24 hours later.

Free grafts will not survive upon the surface of tendon or dense cortical bone, and local hand flaps should be used (Fig. 2), the new raw area thus created being covered by

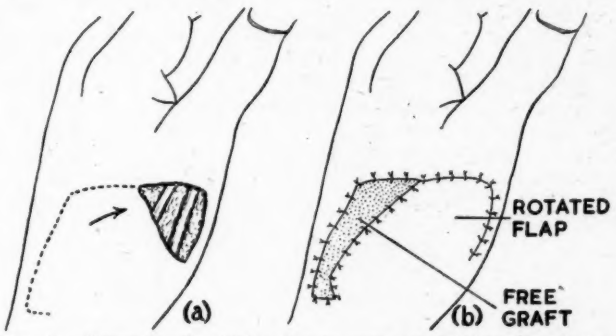


FIG. 2.—Example of rotation flap to cover exposed tendon, bone, or joint.

free split-skin grafting. If the skin defect cannot be closed by local rotation or transposition flaps, a direct flap may be raised at a distant site. The hand is approximated to the upper chest, the abdomen, or the opposite forearm, and a flap pedicle raised and attached in one stage.

Nerve Division

Delayed nerve suture has certain advantages over immediate suture, and there is, therefore, no need to regard nerve division as a surgical emergency. The nerve ends are united by suture of the sheath with very fine stainless steel or tantalum wire, silk, or human hair. It is an operation requiring an adequate exposure in a bloodless field and extreme accuracy of craftsmanship. The results of a satisfactory technical performance can be very good.

In cases of multiple tendon and nerve division at the wrist level, where immediate operation is imperative for the tendon repair, it is helpful to place a single suture through the nerve ends to prevent retraction and shortening of the proximal part.

It should be appreciated that median sensory loss in the hand is more disabling than the motor paralysis; moreover, the latter can to some extent be overcome by suitable tendon transference or tendon grafting, but sensation can return only by nerve recovery. Extensive operations in the hand and forearm to free the main nerve trunks and close gaps between the nerve ends, if necessary by nerve grafts, are amply justified to make the hand "see" and feel again. The ulnar sensory loss is not so disabling as in the case of median paralysis, but the motor loss is much more so. Sensation can be restored by nerve repair up to about five years after injury, but 18 months to two years is about the limit for motor recovery because irreversible changes occur in the motor end-plates.

Tendon Division

Tendon suture or replacement by a free tendon graft can always be performed as a secondary procedure. Its success depends largely upon the general state of the hand and upon the experience of the surgeon. It is not difficult to suture tendons and restore continuity, but it is not always so certain that a sliding tendon and good function will be obtained. Nothing should be done during the initial treatment that may prejudice an already difficult task. Nevertheless, there are occasions when primary tendon suture leads to good results, and while it is not possible to discuss this problem at great length some general indications may be given (see Fig. 3).

Primary tendon repair may be considered if the following conditions are satisfied:

1. The wound has been caused by a reasonably clean and sharp implement; crush injuries may cause more extensive tissue necrosis than is apparent to the naked eye and render primary repair inadvisable. Wounds complicated by skin loss or bone and joint damage are unsuitable.

2. Treatment is instituted within approximately four hours of wounding, but clinical judgment may extend this arbitrary period.
3. Operative conditions are adequate and the correct instruments and suture materials available.
4. An atraumatic technique is employed.

When these conditions are satisfied primary suture may be employed for all extensor tendon divisions.

Primary suture may be used for division of the flexor profundus beyond the level of the sublimis insertion, the flexor pollicis longus in its distal part, and the tendons in the palm, and immediate repair is obligatory for divisions at the wrist level. It is not advisable to perform primary or secondary suture of tendon divisions between the distal palmar crease and the sublimis insertion, for replacement by a free tendon graft at a later stage gives more uniformly satisfactory results.

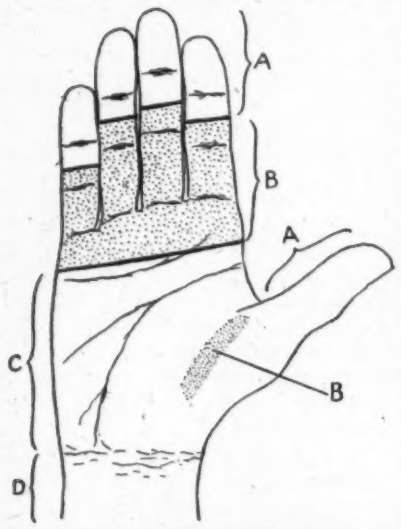


FIG. 3.—Types of flexor tendon division showing suitable methods of repair. A, Primary suture is permissible if general conditions are suitable; otherwise suture skin only and perform tendon graft later. B, Unsuitable for primary suture; suture skin only and perform tendon graft later. C, Primary suture is permissible if general conditions are suitable; otherwise suture skin only and perform secondary suture, tendon transfer, or free graft later. D, Primary tendon suture is always advisable if conditions permit. Perform nerve suture later.

As in all surgery of the hand, fine instruments and a delicate technique in a bloodless field are essential requirements in tendon surgery. The suture material most commonly used is stainless steel wire in single strand, gauge 40, or the twisted form originating in Sweden. The wire is attached to a small straight or curved cutting needle. Stainless steel wire causes less reaction than any other suture material and may remain in the tissues indefinitely without ill effect. Satisfactory haemostasis must be obtained before the wound is closed, as haematoma is one of the causes of deep fibrosis and stiffening of the hand. If adequate haemostasis is secured there is no need to use any form of wound drainage.

Bone and Joints

There is much to be said in favour of the present tendency to use internal fixation, whenever possible, for metacarpal and phalangeal fractures associated with severe lacerations. The need for difficult and restrictive external splintage is avoided, and more attention can be given to the careful repair by grafts or flaps of any accompanying skin loss. Also there is not the same risk of late loss of position requiring further manipulation and disturbance of the healing soft tissues.

Internal fixation may be achieved by the use of carefully fashioned intramedullary bone-pegs taken from the tibia, ileum, or ulna, or by transfixion of the fragments by fine Kirschner wires.

Amputations

The necessity to amputate digits does unhappily arise in cases of extensive lacerations, but it is better to err upon the side of conservative rather than radical surgery. It needs considerable experience to decide whether a severely damaged finger can be restored to usefulness or whether it will eventually become an embarrassment. In our desire to preserve all living tissue in the hand we must not lose our sense of proportion and insist upon preserving digits which cannot be of any use.

When several fingers or the thumb are injured it is wise always to be conservative, because even a part of a digit may be of value to the mutilated hand.

Splintage

After any injury, by accident or by surgery, the tissues must be allowed time to rest and recover. The hand is supported by a compression bandage composed of gauze waste, wool, and crêpe bandage carefully and deliberately applied to give even pressure. The tips of the digits are always left exposed for inspection.

In many instances this bandage will be sufficient splintage, but it is often helpful to apply a simple plaster cover to hold the wrist in slight dorsiflexion. The fingers and thumb, unless there is some special contrary reason, should always be in the position of rest, with the thumb in moderate opposition and the fingers semi-flexed.

The hand, after operation, should be supported in an elevated position for 24–48 hours to assist in the vascular drainage and in the avoidance of oedema.

Next Refresher Course Article.—"Rheumatic Fever," by Professor C. B. Perry.

BICENTENARY OF THE MANCHESTER ROYAL INFIRMARY

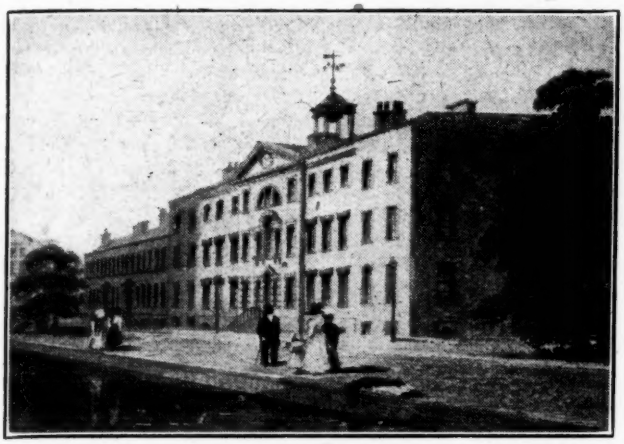
BY

WILLIAM BROCKBANK, T.D., M.D., F.R.C.P.

The Manchester Royal Infirmary first opened its doors on July 27, 1752, 200 years ago, in a little house in Garden Street, off Withy Grove, on the site now occupied by the Co-operative Wholesale Society's building. The house held 12 beds and was staffed by a matron, three physicians, three surgeons, and a secretary. It was called the Publick Infirmary. The government was placed in the hands of trustees. These were persons who had given to the hospital 20 guineas or upwards at one time or were subscribers of 2 guineas or upwards annually.

On the opening day one out-patient presented himself for treatment. A week later the number had increased to five. The first in-patient, a boy of 12 with ulcers on his legs, was admitted on August 3. The number of patients rapidly increased, so that by the middle of October the matron had to be provided with a nurse and a servant. In April, 1753, a room was set aside for an apothecary's shop. In this way began the dispensary, which proved to be a most important feature of the hospital. At the end of a year's work 75 persons had been admitted and 249 out-patients treated, at a total cost of a little more than £400.

At the start of the second year the adjoining house was taken over and equipped with 10 beds. More important was the decision to build a hospital elsewhere, on land now known as the Piccadilly site, situated in open country at the upper end of Market Street Lane. Plans were drawn up for the erection of a building to contain 80 beds for patients, "with proper convenience for nurses and servants and including a hot bath." This "New Infirmary" was brought into use in June, 1755, with 50 beds. The two houses in Garden Street had served their purpose for nearly three years, during which time 374 in-patients and 1,629 out-patients had been handled.



The Manchester Infirmary in 1829, with the adjoining lunatic asylum, on the Piccadilly site.

Having triumphantly launched the infirmary, the board flanked it with a lunatic asylum in 1766 and a complete suite of public hot, cold, and vapour baths in 1780. Persons disordered in their senses were promised "that humane treatment and judicious advice that they had no encouragement to expect in private madhouses." It was also necessary to make a substantial extension to the hospital. It is impossible to stress too greatly the effect of the infirmary on the life of the town at the end of the eighteenth century, due to such far-reaching ideas as the provision of public baths, the introduction of a public health service, the prevention of smallpox, the condemnation of slums, the plea for control of lodging-houses, the investigation of cases of cancer, and the concern about the prevention of accidents in the factories, all in addition to the care of the sick and of those mentally afflicted.

During the first half of the nineteenth century repeated extensions were made, until in 1858 the old infirmary attained its final shape, being surmounted by a dome holding a public clock. The lunatic asylum was transferred to Cheadle and the baths were closed. The final extension was expected to provide an additional 180 beds, but in the calculation the beds had been placed too close to each other. In fact, the gain was only 85, making a total of 277. While these alterations were taking place the infirmary passed its centenary. Since its doors were first opened 940,000 patients had been treated, one-ninth of them in-patients.

Hospital Fever

Hospital fever was a constant worry, and it was hoped that the new wards would lessen its ravages, but this was not the case. To make matters worse the board decided to admit cases of infectious fevers to one of the wings. The routine work of the hospital was maintained by placing the beds closer together until they totalled 310. The inevitable result was a sharp rise in the mortality figures.

A convalescent home was started at Cheadle in 1867 and a fever hospital at Monsall in 1871. But the wards continued to remain unhealthy. The board in desperation called for an independent investigation into the condition of the hospital. The report, dated 1876, disclosed a sorry state of affairs, particularly with regard to the drainage. The modern reader must agree that the only thing to be done was to pull down the building and start afresh elsewhere. There was a suitable plot of land close to the growing university, then known as Owens College. The board proposed this course of action to the trustees, but the trustees would not agree, preferring that the hospital should remain in the centre of the town rather than in its "damp and foggy suburbs." Thus perished the first attempt to move the infirmary from the Piccadilly site. Thirty-two years were to pass before this was finally accomplished.

The board now determined to rebuild and extend the hospital. There was a good deal of land available around the building, but the civic authorities wanted the site for a town hall. Generous terms were offered, but the board could not accept. The city council therefore decided to prevent any encroachment on land not already used for building. The authorities of Owens College endeavoured to persuade the board to move the hospital to Oxford Road, and when negotiations fell through they sided with the city council and effectively blocked successive schemes brought forward by the board. These bodies so influenced the trustees that in 1902 they agreed to the policy that there should be no rebuilding of the infirmary on the Piccadilly site, and ordered that the building and site should be sold on suitable terms and that a new infirmary should be built elsewhere without delay. Thus ended a long and bitter controversy. The members of the board resigned in a body and were replaced by trustees in favour of the new scheme. Within six years the infirmary as we now know it had been designed and built. It was ready for occupation in the autumn of 1908, and on a raw foggy December morning the patients were transferred to the new building. No time was lost in demolishing the old infirmary, its place being taken by a lovely garden where the townsfolk can sit and rest in the centre of the busy city. May it always remain thus.

The New Building

The new building, designed to hold 500 beds, with accommodation for an additional 100 if needed, was formally opened on July 6, 1909, by their Majesties King Edward VII and Queen Alexandra. The chairman of the board of management (Mr. William Cobbett) read an address of welcome and was knighted on the spot. Thereafter the board pursued through peace and war a remarkably progressive policy. Even the extensive damage wrought in two air raids in 1940 was not allowed to interfere, and in the darkest days plans were laid for the big developments which subsequently took place.

Many famous men have served on the medical staff of the infirmary. Charles White is renowned in the history of midwifery. Thomas Percival's medical ethics are still well known and respected. John Ferriar did much to develop public health services in the rapidly growing township. Peter Mark Roget wrote the *Thesaurus* beloved by addicts of the crossword puzzle. Edmund Lund introduced Lister's principles into the hospital. Walter Whitehead left his name in the annals of surgery. William Thorburn was a pioneer in neurosurgery. Graham Steell and James Ross made outstanding contributions in cardiology and neurology respectively. R. T. Williamson's book on the spinal cord is a classical work and is still in use. Lloyd Roberts, William Milligan, Archibald Donald, and Alfred Barclay developed their specialties within its walls. Arthur Burgess showed the practical possibilities of dealing surgically with acute abdominal emergencies. E. D. Telford laid the foundations on which vascular surgery has developed. John Morley, Geoffrey Jefferson, and Harry Platt have added greatly to its prestige, and the tradition is being worthily maintained. Lord Moran, Lord Webb-Johnson, and Sir William Fletcher Shaw, presidents simultaneously of the three Royal Colleges, all studied in the Manchester Medical School.

On July 5, 1948, the board of management lost control of its infirmary, which passed into the care of the board of governors of the United Manchester Hospitals under the chairmanship of Mr. Colin Skinner, who had been its treasurer for nearly 20 years. No happier or better appointment could have been made. Since the appointed day there have been many serious problems, including the amalgamation of the five constituent hospitals and the co-ordination of the services they provide with those provided by the hospitals belonging to the regional board. In addition, the rapid advance of scientific methods in medicine has necessitated the provision of much more adequate facilities.

In spite of increasing economic difficulties steady progress has been maintained. The neurosurgical block was opened in 1950 by Lord Webb-Johnson. More important still was the approval given by the Ministry to the erection of a big new building for radiology and clinical pathology, two vital and rapidly expanding departments that are badly hampered by cramped accommodation.

Thus the Manchester Royal Infirmary has kept and is keeping pace with the astonishing advances made in medicine during the past two decades. In many fields it has led the way, and it can truly be said that the hospital has a world-wide reputation as a centre of treatment and research and as a teaching school.

A.C.T.H. AND CORTISONE IN RHEUMATIC FEVER

A preliminary report of an international study of the relative merits of A.C.T.H., cortisone, and aspirin in the treatment of rheumatic fever was made recently in Chicago. The results of the study are at present inconclusive. The work is being conducted in 13 research centres in the United States, Great Britain, and Canada by the American Heart Association's Council on Rheumatic Fever in conjunction with the Medical Research Council. British representatives on the panel which made the report were Professor A. Bradford Hill and Dr. E. G. L. Bywaters.

The plan of study provides for uniform criteria for the diagnosis of rheumatic fever and for the degree of rheumatic activity required for the admission to the study, the random allocation of patients to the three treatment groups, a defined dosage schedule of the drugs for a fixed period of time, a specified period of observation following treatment, and a long-term follow-up schedule. It also lays down precisely the frequency and type of clinical and laboratory observations to be carried out on each patient. To date, in all three countries, 658 cases have been admitted to the study, and the analysis of rather less than half of these is the basis of the preliminary report. So far no consistent pattern of response to treatment is evident, and no firm conclusions can at present be drawn concerning the drug most effective in the control of the acute illness. The cases have not been under observation sufficiently long to provide data on the prevention of rheumatic heart disease. Admission of new cases to the study will be brought to an end later this year. It is expected that a total of 750 cases will be available in all three countries for final analysis.

BRITISH EMPIRE CANCER CAMPAIGN

Delivering his presidential address to the 29th annual general meeting of the British Empire Cancer Campaign at the House of Lords on July 3, the DUKE OF GLOUCESTER announced that the Queen had graciously consented to grant her patronage to the Campaign. The new report, the Duke went on, "gives clear proof of the remarkable activity of the Campaign at home and overseas . . . the headings alone show plainly the extraordinary amount of hard work done by the council and committee of the Campaign . . . and the many devoted men and women working patiently in their laboratories and at the bedsides of the sick." The Duke of Gloucester also commented on the increasing liaison between the Campaign and research establishments in Canada and the United States, and said that the Exchange Fellowship system was "operating steadily and smoothly."

Proposing a vote of thanks, the chairman, Lord HORDER, gave as an example of the Duke's practical interest a message which he had sent to a cinema in Jersey, where a film *première* was being held to raise funds. This message crowned the success of the function, which raised £2,500 for the Campaign.

Moving the acceptance of the annual report (see also p. 84), Sir DANIEL DAVIES drew attention to a newly published book entitled *A Study of Cancer in London*, which surveys the work of all London hospitals treating and diagnosing cancer over a five-year period ending in 1944. It covered 15,201 cases. All but 400 had been followed up. Only 29% of the cases were at a localized stage on coming for treatment; however, of 451 stage 1 cases treated by surgery and radiotherapy, 55% were still alive after five years. This once again showed the vital need for early diagnosis. With this, Sir Daniel coupled a plea for intelligent education of the general public about cancer. Seconding the report, Mr. J. C. BURLEIGH, of the Finance Subcommittee, said that the British Empire Cancer Campaign's income for the past year from donations, collections, and legacies had been nearly £260,000—over £34,000 more than in 1950.

Reports of Societies

TREATMENT OF ANURIA

At a meeting of the Section of Urology of the Royal Society of Medicine, on June 26, Dr. E. M. DARMADY opened the proceedings by reminding the audience that considerable advances had been made in the understanding of the anurias since he addressed the Section four years ago. The advances were due to a better knowledge of the pathology and natural history of the disorder, and of methods of combating the toxaemia of renal failure.

Whatever the cause of acute tubular necrosis, the most important factor was circulatory failure. The kidney was profoundly affected by anoxia, and could not remain severely ischaemic for more than six to eight hours without developing changes which were often irreversible. Dissections of the nephron by Oliver and his own group showed that the characteristic changes (irrespective of the aetiology) were disruption of the tubular wall and patchy degeneration of the tubular epithelium, which affected the upper as much as the lower nephron. There were three stages in the natural history of the syndrome, as described by Bull and his colleagues: the onset, which usually lasted about six hours after the initial stimulus, the stage of oliguria or anuria, which might last for up to 22 days, and finally a late diuretic phase during which large amounts of water and electrolytes were lost.

The causes of the precipitating circulatory failure were manifold and were difficult to classify, but might be divided into general causes (shock, trauma, etc.); reflex causes (calculus anuria, vascular injury, sulphonamide anuria, etc.); renal diseases, such as nephritis; allergic causes; and various toxins. Obstetrical accidents such as ante- and post-partum haemorrhage were also of great importance.

In treatment, splanchnic block and intravenous diuretics such as sodium sulphate were likely to succeed only if adopted at the very onset. The essence of treatment lay in the control of circulatory failure and fluid intake, and restriction of the accumulation of waste products. The last factor could be dealt with either by removal of the waste products by some form of dialysis, or by minimizing their formation. Assessment of cellular and extracellular hydration was often difficult, and, although estimation of the haematocrit and plasma specific gravity were helpful, measurement of the osmotic pressure of the plasma by the method of Hamburger was more promising. In the anuric stage overloading with salt and water was disastrous, and new methods of estimating the volume of the extracellular compartment were urgently needed. The late diuretic phase often occurred suddenly, and necessitated rapid replacement of water and electrolytes. Since hypokalaemia was likely to occur at this time it was helpful to have readily available stock solutions containing potassium (1.9% potassium lactate or 1.1% potassium chloride).

Dr. G. M. BULL said that anuria was due to three main causes: circulatory insufficiency, organic renal damage, and obstruction. He and his colleagues, Dr. A. M. Joekes and Dr. K. G. Lowe, had studied 112 cases of anuria or severe oliguria at Hammersmith Hospital from 1947 onwards: 48 were due to circulatory renal insufficiency, 59 to organic

renal disease, and 5 to obstruction. The last type of case had been infrequent in this series because they were usually referred direct to the surgeon. The usual cause of circulatory renal failure was severe dehydration or haemorrhage, but occasionally it was heart failure. The common factor was failure of the general circulation leading to renal vasoconstriction which resulted in ischaemia, and if severe and prolonged this could cause tubular necrosis. Circulatory renal insufficiency superimposed on organic renal damage was common, and hence it was vital to restore the general circulation, but obstruction must always be ruled out.

The essentials of the conservative management of the syndrome were a careful water and electrolyte balance and a high calorie mineral- and protein-free diet, with the fluid intake restricted to 1 litre of fluid per day plus the volume of urine passed in the previous 24 hours. Some special points in treatment required mention: anaemia was a common finding, and the haemoglobin level should be kept above 70% by transfusion of packed red cells. When vomiting precluded the use of oral feeding, infusion of a 40% glucose solution containing heparin through a polythene catheter passed into the superior vena cava via an antecubital vein was a suitable alternative. Hyperkalaemia might occur as a result of excessive cell breakdown; dialysis was a complicated and often dangerous method of treatment, but the serum potassium level might be temporarily lowered by the intravenous injection of insulin and glucose, followed by feeding a cation exchange-resin in the sodium cycle. The routine administration of potassium citrate in urological wards should be avoided. In the diuretic phase hypokalaemia could be treated by a liberal intake of fruit, or potassium given by mouth as the chloride in doses not exceeding 5 g. daily. Infection frequently caused death in anuria, and penicillin should be given as a routine. Failure to excrete penicillin ensured an adequate blood level from one dose of 1 mega unit in cases of complete anuria. For the same reason other antibiotics which were excreted by the kidney (e.g., streptomycin) and which were capable of producing toxic effects should be given in reduced dosage.

Surgical Measures

Mr. ASHTON MILLER mentioned surgical measures for the relief of anuria, before passing on to discuss the obstructive types. Renal decapsulation was an ineffective and unjustifiable procedure, since it neither relieved increased intrarenal tension nor resulted in renal sympathectomy. Once anuria was established sympathetic block was of no value. In speaking of the obstructive anurias he said that ligation of the ureter produced transient pain in the loin and slight hydronephrosis, but that the kidney would function again if the obstruction were relieved in 14 days. Pyonephrosis did not always occur if the kidney was previously infected.

In anuria following blockage of one or both ureters by calculi, obstruction was most common in the upper third of the ureter and was followed by colic, a palpable tender kidney, and muscular rigidity over the affected kidney; a radiograph usually showed the calculus. Occasionally atypical cases were seen in which these signs were absent, and in these cases the teaching of the older surgeons to operate on the side on which the pain was last felt had much to commend it. The obstruction was rarely total. It was essential always to perform a cystoscopy and ureteric catheterization in order to confirm the site of the obstruction before operating for its relief. Usually relief of the obstruction led to a rapid return of urine flow. If the catheter pushed a calculus up into the kidney it was wise to defer operation until the patient's general condition had improved as a result of the diuresis. If the catheter bypassed a calculus and established a flow of urine it was better to remove the stone by open operation at the same sitting rather than leave the catheter in-dwelling alongside the stone.

Reflex anuria was described as a "blunderbuss term" which was used in too loose a sense, since there did not appear to be any experimental evidence to support a reno-renal reflex. When a stone blocked one ureter completely the other kidney might temporarily cease to function from circulatory causes resulting from dehydration and vomiting, but this was not really reflex anuria. Sulphonamide anuria was still quite common in dehydrated individuals—particularly children—but crystals were rarely found, and the anuria often had some of the characteristics of acute tubular necrosis. Sulphonamide obstructive anuria and sulphonamide tubular necrosis were probably different degrees in the same disease. Obstruction of the ureters from pelvic neoplasms often caused sudden anuria. When the ureters were obstructed after gynaecological operations, pyelostomy should be performed at once, the ureters being re-implanted in the bladder at a later date. Occasionally such cases were seen by the urologist less than 48 hours after the operation, and in this event exploration of the operation site might be undertaken.

Discussion

The communications were discussed by Mr. G. J. SOPHIAN, who reviewed the evidence in favour of the Oxford shunt, and by Dr. R. H. PARAMORE, who made a plea for spinal analgesia in the treatment of anuria. Contributions to the discussion were also made by Mr. A. W. BADENOCH, the president, and several other members of the audience. In the summing up Dr. BULL said that the three opening speakers had between them collected 36 cases of anuria resulting from acute tubular necrosis which had been uninfluenced by renal sympathetic interruption.

Nova et Vetera

THE SCIENTIFIC DISCIPLINE

New Worlds and Old. By Charles Singer. (Pp. 178. 15s.) London: William Heinemann Medical Books. 1951.

We are indebted to Professor Singer for reprinting these informative and fascinating essays, which are assuredly too significant to be forgotten. His role among our historians of science is that of the observer who is more concerned with general philosophical trends than with the minutiae of the study. Not that the latter are ignored or beyond his reach—witness his recent *Prelude to Modern Science*, in which the miniaturist plays a revealing and impressive part. Nevertheless he cannot resist an occasional dig at those abstruse and purblind enthusiasts with whom detail is all-sufficing. Such "dull, obstinate, timid, or temporarily limited beings," he says, cannot realize that science is a great deal more than that.

The essays cover a considerable and varied ground, such as the world of Copernicus and Vesalius; Robert Hooke; the dawn of the scientific age; science and religion; Theophrastus; Galen; and Francis Adams—a great country doctor. The last-mentioned essay, though by no means the most important, is perhaps the most attractive. In it Singer himself appears in an openly appreciative light, and writes of his subject in terms of deep affection and unreserved admiration. It is a discourse to be read and remembered by all his friends. Those who have not followed the findings of recent classical research will be surprised to learn that Hippocrates is the King Arthur of medical history. His bare existence must be admitted, but of his personality and works nothing but dubious legend is available, and there is not even any evidence that he was responsible for a single item of the Hippocratic Collection. His portrait in fact embodies the attributes of the ideal physician, but of no specific person.

In these essays Singer dwells particularly on the importance and outstanding influence of the scientific discipline on man and his civilization. Science, we are told, has opened up "a great new world in which the spirit of man may endlessly rejoice and refresh itself." On the more biographical side it need only be said that Professor Singer has contrived to throw new light on all the major sources relevant to his theses.

F. J. COLE.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Change of Colours of Gas Cylinders

SIR,—For some years past the Medical Defence Union, the Association of Anaesthetists, and the British Oxygen Company, acting under the aegis of the British Standards Institution, have sought measures to eliminate accidents in which the wrong anaesthetic gas is given to a patient. After many conferences on the subject agreement has been reached, and shortly action will be taken. There still remains the possibility of introducing a non-interchangeable valve that would render it wellnigh impracticable for an anaesthetic apparatus to be rigged in the wrong manner to give the wrong gas. This awaits further conferences and agreements. For the present, however, the following changes are imminent in the colour markings of gas cylinders.

1. In the past manufacturers have followed a particular scheme in colouring the outside of cylinders containing medical gases to enable anaesthetists and others readily to identify the gaseous contents, or to select a cylinder containing the gas or mixture it is intended to use. The colours that have been applied to cylinders in this country hitherto conflict with those used for similar gases in other countries, and, as a result, certain serious errors and some fatal accidents have occurred. Anaesthetists have been confused by the use of different colour marking by manufacturers in countries overseas when their cylinders and ours have been intermixed in hospitals and other medical units at which practitioners of two or more nationalities are employed.

2. As a step towards the removal of this danger a high measure of agreement has been reached on an international basis on the standardization of colours, names, and symbols of medical gas cylinders, and this involves an alteration in the identifying colours of most of the cylinders at present in use in the United Kingdom.

3. To accord with the new standard these alterations of colour will be effected by the suppliers, who have devised a comprehensive scheme for the collection and repainting of cylinders in a short period of time.

4. A special effort of co-operation between suppliers and users will be necessary to reduce to a minimum the time taken to effect a complete change-over and to recognize the risk arising from a user having temporarily cylinders of two different colours containing the same gas.

5. To avoid confusion and danger all cylinders containing one particular gas will be dealt with *seriatim*; the first batch of cylinders to be altered in their colouring will be those containing **Nitrous Oxide**, all of which are at present painted black. They will be changed to **French Blue**. The repainting of the nitrous oxide cylinders will commence on August 1. Prompt information must be given to the supplier now, and throughout the operation, as soon as empty cylinders are ready for collection. If, however, any nitrous oxide cylinders held by a user are not likely to become empty in the immediate future the supplier should be informed and arrangements made for these to be collected, credited, and/or replaced.

6. After the manufacturers have dealt with the repainting of cylinders containing nitrous oxide the repainting of cylinders containing other gases will begin. Hospitals will receive instructions from the Ministry of Health, and further particulars will be issued by the suppliers regarding the collection of cylinders containing other gases, when they are ready to deal with them.

7. During the transitional stage and for a considerable time thereafter it will be necessary to identify the gas contained in any cylinder by reading the name of the gas or the chemical symbol appearing on the cylinder, as only thus will accidents be avoided.

8. A new colour chart will be issued to hospitals, and is now available to any who desire copies on application to the British Standards Institution, 24, Victoria Street, London, S.W.1.

9. Hospital authorities are being invited to designate a responsible administrative officer in each hospital to take action on the following lines:

(*a*) A notice should be prepared in the following terms and prominently displayed in every part of the hospital where gas cylinders are handled or gas is used; personal copies should be handed by the administrative officer to every doctor, dentist, nurse, and midwife engaged in the hospital, and to all porters and others persons who handle gas cylinders:

> "Starting on August 1, changes will take place in the colouring of medical gas cylinders; to identify the gas, reliance must be placed primarily on the name of the gas or the symbol stencilled on the cylinder, and not on the colour of the cylinder."

This action should be taken shortly before the date indicated in the notice, and the administrative officer should obtain the signature of each person receiving a personal copy, in token of having received, read, and understood it.

(*b*) The administrative officer should be responsible for seeing that all new staff engaged are similarly handed a notice and required to sign for it.

(*c*) He should see that every medical gas cylinder arriving in the hospital, and every cylinder already in stock, has attached to it immediately a red tie-on tally bearing the words in heavy black type:

DANGER, COLOURS ARE BEING CHANGED. READ THE LABEL AND CHECK THE SYMBOL AND NAME OF GAS.

It will be the duty of the hospital authority to see that frequent inspections are made by the administrative officer to ensure that the tallies are in position on all cylinders used at the hospital.

10. Any person about to use a medical gas must first satisfy himself of the identity of the gas he selects to administer to a patient. A person using an anaesthetic machine should always verify the couplings of the apparatus before starting to use that machine. Safety of practice can be achieved only if everyone undertaking to administer a medical gas observes the following rules:

A. Read the name of the gas or symbol on the cylinder.
B. Check the coupling of the anaesthetic apparatus.
C. Test the gas for identity at the delivery-end.

—I am, etc.,

ROBERT FORBES,
Secretary.
Medical Defence Union.

Watch for Malaria in Britain

SIR,—We are engaged in a war in which our troops are fighting in malarious theatres (Korea and Malaya), whilst others are stationed in more peaceful malarious places such as West Africa; the incidence of malaria in all these theatres is within reasonable bounds and on the whole is surprisingly low. Various preventive measures are used, but considerable emphasis is laid on "paludrine" as a prophylactic, the experiences with which have been satisfactory.

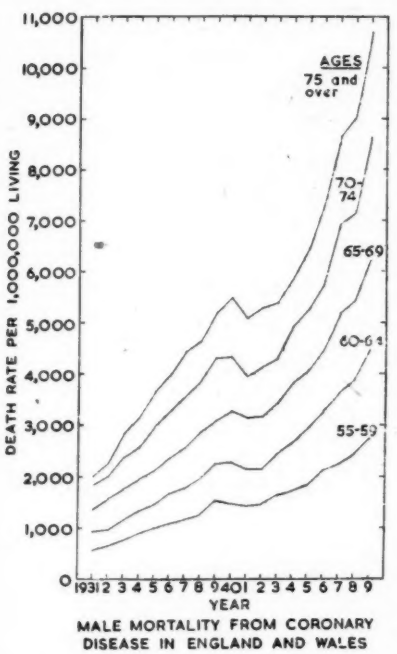
Paludrine, in common with other drugs, may only act as a suppressant of benign tertian malaria, and clinical attack may occur when it is discontinued. Benign tertian malaria is the predominant malaria of Korea, and it is therefore to be expected that a number of attacks of malaria will occur amongst soldiers who have returned from that theatre. The numbers recorded are low, the total in this country last year averaging only 16 per month, and, the disease being benign, there is no immediate grave risk to the individual. It is, however, inevitable that some of these soldiers will suffer relapses after demobilization, which may occur quite quickly after their return from Korea, and it has been brought to my notice that a number of cases amongst demobilized men have only been diagnosed after prolonged examination and treatment for other disease, neither the doctor nor the patient having considered the possibility of malaria.

A strongly worded warning of the possibility of a relapse is given to soldiers on their return, but in the cases referred to this mechanism has failed for one reason or another to put men on their guard. If practitioners meet cases of acute febrile illness amongst recently demobilized men they should bear the possibility of a malarial relapse in mind, seeking an early confirmation of the possibility, either by referring the patient to an appropriate hospital or by arranging for the rapid examination of blood films.—I am, etc.,

G. MACDONALD,
Hon. Consultant in Malariology to the War Office.
Ross Institute of Tropical Hygiene, London, W.C.1.

Cholesterol Tolerance and Coronary Thrombosis

SIR,—I feel that Dr. Ian Wang's statement (June 14, p. 1278) that "the present restrictions on the diet of the British population has not reduced the number of deaths from coronary thrombosis" requires some amplification. There was a definite discontinuity in the death rates of England and Wales from "diseases of the coronary arteries and angina pectoris" (group 94 of the *International Classification* (5th Revision, 1938)) during the war years; these death rates (Registrar General's *Statistical Review*, Text, Volume I, Medical 1946–7, p. 199) for males are shown in the diagram for quinquennial age groups. It will be seen that, in general, there was a fall in 1941, after which the upward trend was resumed, but not until about 1947 did the rates reach the level which would have been attained had the upward trend of 1931 to 1940 continued without interruption. The rates for females are considerably lower than for males, but show the same features.



MALE MORTALITY FROM CORONARY DISEASE IN ENGLAND AND WALES

While some of the increase in coronary disease mortality may be due to changing fashions of certification or accuracy of diagnosis, it does not seem reasonable to ascribe the wartime "trough" to this cause. However, additional evidence is needed before the discontinuity can be said to be caused by the low cholesterol content of the diet, rather than by some other of the many wartime changes in living conditions.

Of the two other large groups of degenerative heart diseases, "cardiovascular degeneration" (group 93, c.1) shows a pre-war increase and a more pronounced wartime trough than does coronary disease, while the rates are still far from reaching the level found by continuing the pre-war trend. "Other myocarditis (not acute, hypertensive, or arteriosclerotic)" (groups 93 c.3 and 93d) does not appear to show any sort of wartime trough. It is also interesting to note that the death rates for "cerebral embolism, thrombosis, and softening" (groups 83 b, c) show similar features to those for cardiovascular degeneration.

It is, of course, rather dangerous to draw conclusions from the trends of recorded mortality by cause of death owing to changes with time in the practice of classification and diagnosis, but it does appear that there was some influence at work during the war years which tended to reduce deaths from heart disease, and that this influence had more effect on diseases classified as cardiovascular degeneration than on coronary diseases. Cholesterol may have had something to do with the reduction, for in Sweden and other Scandinavian countries, where the cholesterol content of the diet fell during the war, the heart disease death rates also fell, while in the U.S.A. the cholesterol did not fall and heart disease mortality continued to increase (Malmros, H., *Acta med. scand.*, 1950, Suppl. 246, p. 137).

It is hoped to discuss fully the trends and variations of heart disease mortality in a paper to be submitted to the *Journal of the Institute of Actuaries*.—I am, etc.,

Harrow, Middlesex. R. H. DAW.

SIR,—I should be pleased if you would give this letter some publicity on account of its potential importance in the dietary treatment of coronary thrombosis. Dr. Ian Wang (June 14, p. 1278) has shown that *crystalline* cholesterol has little effect in elevating the level of serum cholesterol. This is not surprising, seeing that cholesterol in such a form is poorly absorbed by the human (Cook and Edwards, *Biochem. J.*, **49**, xli). If cholesterol is given in the form of eggs absorption is good (Cook, Edwards and Riddell, to be published). Cöllen, de Kruif, and Geier (*Permanente Fdn. med. Bull.*, **7**, 55) have shown that there is a rise in the level of plasma cholesterol two and four hours after the ingestion of 250 g. of egg yolk (about 5 g. cholesterol).

It is my considered opinion that the consumption of large quantities of eggs is dangerous for coronary patients. It is not normal to consume crystalline cholesterol.—I am, etc.,

Biochemistry Department, University College, Dundee. R. P. COOK.

Oesophageal Ulcers Near Aorta

SIR,—The medico-legal report, "Fatal Bread Crust," in the *Journal* (June 21, p. 1361) reminds me of a somewhat similar case which, although without a legal aspect, is not without interest.

During the war years Mrs. X, aged about 70, while eating stewed plums swallowed one of the stones, which caused her considerable pain and discomfort. She vomited the stone, and it was assumed that the matter was concluded. However, she still got pain and dysphagia which it was not possible to relieve. About a fortnight or three weeks later, however, she vomited another stone and a quantity of bright red blood. Pain continued and she was admitted to hospital for investigation. A radiograph showed an ulcer of the oesophagus over the spot where it crosses the arch of the aorta. In the meantime vomiting of blood got worse, and it was assumed that she had an ulcer which was boring into the aorta. Urgent treatment was of course necessary, and a gastrostomy was performed, with more or less immediate relief of her symptoms. After two or three months the gastrostomy was closed and she made an uninterrupted recovery.

The interest is that this lady swallowed two plum stones and an acute ulcer of the oesophagus resulted, which without energetic treatment might easily have proved fatal.—I am, etc.,

Petworth, Sussex. D. C. DRUITT.

Unusual Case of Obstructive Jaundice

SIR,—The following case is worth recording because of the unusual cause of obstructive jaundice.

Two years ago a woman aged 57, married, with four children, was sent to me by her own doctor on account of jaundice which he thought was due to a stone in the common duct. Several months prior to admission to hospital the patient had had an attack of acute cholecystitis. Under appropriate treatment the acute inflammation, which was apparently severe, subsided after about seven days. According to the doctor, there was no history of flatulence or of gall-stone colic prior to the attack. Since that time he had never seen the patient until the day before her admission to hospital. She then complained of severe abdominal pain and a feeling of malaise, and looked yellow.

I elicited that since the attack of acute cholecystitis she had had a history of flatulent dyspepsia punctuated by bouts of abdominal pain. The pain, however, did not seem to have the severity of gall-stone colic. Jaundice appeared for the first time about seven weeks prior to admission. At first it appeared to be of the intermittent type, but in the last two weeks deepened without intermission. The abdominal pain also became more or less constant, and the patient's appetite was considerably diminished. She looked toxic, markedly jaundiced, and was tender over the liver; the gall-bladder could not be palpated. There was intermittent fever, but no rigors.

Owing to the history of acute cholecystitis, I made a preoperative diagnosis of a stone which passed from the cystic to the common duct. Owing to the absence of flatulent dyspepsia prior to the attack of acute cholecystitis, I thought the stone might be metabolic, and not infectious, in origin. If, however, the patient's story were true, my interpretation of the sequence of events would not explain the absence of genuine gall-stone colic.

At operation, through a Kocher incision, the omentum was densely adherent to the liver. When the under surface of the

liver was exposed after division of the omentum the gall-bladder could not be seen. Instead, a strong peritoneal band nearly 1 in. (2.5 cm.) thick was seen to stretch from the duodenum to a hard knob (presumably the gall-bladder) which appeared to be incorporated into the liver. When the band was divided a spring was released and, like a jack-in-the-box, the gall-bladder appeared for the first time. It was not much bigger than the distal phalanx of the thumb. It was markedly contracted. No stones could be felt in it or in the biliary passages. The pancreas was normal in size and consistence. There was no evidence of cirrhosis of the liver. The common duct was opened and, along with the common hepatic duct, was explored with a negative result. The common duct was afterwards drained. The bile was dark green in colour. In my opinion, the jaundice was due to a kinking of the common duct by the thick peritoneal band which I divided. The band was the result of the previous cholecystitis, which was apparently not associated with gall-stones.

The jaundice completely disappeared before the patient left hospital. With the exception of one attack of abdominal pain, she has remained well ever since the operation.

"The hepatic or common bile ducts," writes Sleigh Johnson (in R. Maingot's *Postgraduate Surgery*, p. 763, Medical Publications Ltd., 1936–7), "may uncommonly be involved in an innocent chronic perihepatitis with gross fibrinous thickening of the capsule which with organization and subsequent contraction of fibrous tissue grips the ducting in a ring of cicatricial stenosis or *kinks* them in their course. *Local peritoneal adhesions around the gall-bladder or duodenum may rarely produce a similar obstruction*" (all italics mine).

I am indebted to Captain Quigley, the Curragh Military Hospital, for his assistance.

—I am, etc.,

Curragh, Eire. D. J. CANNON.

"Negligence" in Hospital

SIR,—Your interesting leader (June 21, p. 1341) ends with the words, "In future, therefore, it would appear that any prospective plaintiff who is aggrieved by his treatment in hospital need bring his action *only* (my italics) against the hospital authority, which will be equally responsible whether it turns out that his injury was caused by the negligence of a nurse, a house-surgeon, or a consultant." Experience over the last few years shows that such prospective plaintiffs invariably do bring their actions against the hospital authority concerned, mainly because, as an employer, the hospital authority is vicariously liable for the negligent acts of its employees in the course of duty.

However, the liability of the State to pay damages if such negligence is established is not an exclusive liability, and the doctor who is alleged to have been negligent is not relieved from personal liability. In practice he is almost invariably sued concurrently, since the plaintiff gains certain technical advantages in having him as a defendant. Unhappily the matter does not stop there, because the Ministry of Health has declared it to be its policy that hospital authorities should, if it is sought to make them liable for negligent acts of any doctor on the staff (and it matters not whether he is a consultant, either whole-time or part-time, or of more junior status), take such steps as are open to them under the Law Reform (Married Women and Tortfeasors) Act, 1935, to obtain a contribution from the doctor in respect of damages that may be recovered. Under the Act such contribution may amount to a complete indemnity.

Thus every member of a hospital medical staff should remember that he cannot safely rely for his defence upon a hospital board, whose interests will usually conflict with his own. Not only does the State not relieve him of the burden of liability in such cases, but under the Ministry's policy it assumes the role of assailant. A doctor who may find himself involved in a complaint which may lead to legal proceedings by an aggrieved patient for damages should therefore immediately consult his protection organization, and certainly he should not give any statement to his hospital authority or anyone else before seeking such advice.

Any reader who is further interested in the operation of the Ministry's policy and the doctrine of vicarious liability should read the judgments of the Court of Appeal reported in *The Times*, May 30, under the heading, "Negligence in a Hospital: Apportionment of Liability."—I am, etc.,

ALISTAIR FRENCH,
London, W.C.2. Secretary, Medical Protection Society.

SIR,—Your leading article on the subject of negligence in hospitals (June 21, p. 1341) focuses attention on a problem of no little importance. By a series of decisions in the English courts it is apparent that the Ministry of Health as the hospital authority is responsible at law for the acts and omissions of the medical staff, including the consultant staff, of hospitals, a position which has apparently been accepted without obvious misgiving by consultants in England. The position in Scotland prior to the National Health Service (Scotland) Act, 1947, was that the legal responsibility for clinical work in hospital rested on the consultants, the hospital authority acting merely to bring patient and doctor together; thus the hospital consultant could act with complete professional freedom according to his discretion, accepting legal and, in the end, financial responsibility for his actions. The incorporation in the Scottish Act, under Section 70, of the provisions of Section 116 of the Public Health (Scotland) Act of 1897 seems now to make the State responsible for the acts and omissions of hospital staffs in Scotland, a situation which obtains in England both by the provisions of the English Act and by legal decisions before and after the passing of that Act. As yet no decision in a Scottish court has affected the status quo, but it is considered unlikely that this position can be maintained.

The purpose of this letter is to draw the attention of the profession in hospital practice to the risks inherent in this situation. It is all too easy to imagine circumstances developing to the extent that hospital authorities, including the Department of Health for Scotland and the Ministry of Health, lay down rules for the conduct of clinical work. No matter how unlikely it may at present seem that such dangers may be translated into specific cases of interference by hospital management boards, regional hospital boards, or Government departments in matters correctly falling within the realm of professional decision, the situation appears to be one which calls for careful thought and action on the part of the profession.—I am, etc.,

Edinburgh. J. G. M. HAMILTON.

Family Advice

SIR,—I am extremely grateful for the letter from Dr. Gwyneth M. Cotterell (June 14, p. 1302) asking if there is any way of obtaining information about doctors, midwives, hospitals, and nursing-homes interested in "natural childbirth." I have been up against much the same problem both in a personal way and as honorary secretary of my local Marriage Guidance Council. I have recently had cause to inquire into facilities of this kind on behalf of two expectant mothers, one in the West of England and one in the North: their local doctors were unable to help them, and there was no suitable hospital accommodation available.

I am glad that some general practitioners and public health authorities are alive to the growing demand for more understanding preparation for childbirth, and that some hospitals have excellent antenatal departments. But there are many where this is not so, and I believe still more where the antenatal work is not logically followed up in the labour ward.

I would like to back up Dr. Cotterell's proposition that a register of sympathetic hospitals and nursing-homes be kept, and also that there should be a list of midwives available for private nursing of this kind. One hopes, too, that members of our profession will appreciate more fully the increasing demand for understanding cooperation between mother and doctor in this tremendously significant experience of childbirth.—I am, etc.,

Croydon. O. CYNTHIA HARRIS.

Family Planning

SIR,—One has hesitated to enter the realms of world problems as related to the present family planning (F.P.) arguments, feeling it to be a region where even highly informed experts of practically angel status would fear to tread, but still hoping that someone with sufficient knowledge to present it would give a view of the side of the

picture other than that already presented (mainly by medical and lay Family Planning Association (F.P.A.) participants, who, understandably enough, are anxious to defend their present positions in the association).

Drs. Malleson, Dovey, and Pyke feel that an increased interest in F.P. shown in this country (sponsored, of course, by as many members of the profession as possible) would point the way to less enlightened races to help to reduce their food problems in reducing their numbers.

I feel that Dr. Pyke, as an F.P. representative (commenting on a recent W.H.O. meeting), has rather let his team down in remarking on the utter lack of approval shown by various world delegates on the question of birth control as a subject for serious international discussion. His wide-eyed astonishment at the very sensible comment of the Austrian delegate is noteworthy; as are also his comments on voting "in principle," and the question of "religious sensitivities." But the climax comes when we hear of a resolution passed by the British F.P.A. that it regrets the United Kingdom delegate to W.H.O. did not indicate "the feeling of the majority of the people of this country that birth control advice should be made available to those who need and desire it" (the latter verbs being conveniently ambiguous if together). What census he took of the "majority of people" and how well qualified such people were to judge we have no way of knowing. But it comes as rather a shock to realize that such statements are apparently made as representing a country's views while many of us are completely uninformed of them.

Let us, however, take the F.P. argument at its face value. The tempting, though superficial, attitude to take to this "Let's show the over-populated countries how to do it" slogan is as follows. Unless we take steps to get an ample supply of young healthy British stock and transplant it to our self-subsistent Commonwealth, which can feed us all, it is very possible that the rapidly increasing underfed Eastern nations, far from emulating any F.P. programme (they are gradually realizing that there is *strength* in numbers) will by sheer weight of their numbers be tempted to enter and occupy the invitingly unpopulated areas of our Commonwealth for us.

To take the suggestion seriously, however—especially anent the world food situation—either the increase in the world's population as a threat to world food supplies is an urgent problem or it is not. *Re* the latter, there are many who can show that the world could, even with increase, easily feed itself, but will not organize nationally or internationally to that end. The whole subject is too complex, however, to be easily dealt with in a short space. A point, though, that would-be controllers of population should bear in mind is that the raising of the world standard of living, education, and health, which we all hope for, will automatically bring with it the voluntary and unassisted control of conception which races such as our own are already rather seriously exhibiting.

If, however, we agreed that the filling of human stomachs is a problem which present increase in world population is going eventually to render impossible, then this is a matter of the most grave urgency which should be dealt with immediately. Dr. Pyke informs us that India on its own is contributing a fifth of the total world population increase (20m.) in a year.

Obviously then, if F.P. is the answer, it is of the utmost urgency that all present F.P. clinics here be transferred forthwith to India, where they can act promptly as missionaries, on the most vital of all missions. Should the Indians resent such intrusion—or be too slow to take the matter up themselves—then would it not be up to our planners to bring down our own population increase to nil in the hopes that a proportionate number of hungry Eastern mouths be fed? Or, more logically still, that we sterilize all our people of reproductive age so that overcrowded and underfed foreign peoples of the future might have our lands to occupy and more food whereon to feed themselves?

The moral, of course, is that if the planners must suggest interference by attempting artificially to control world population increase, then it is high time we clarified our views as to which nation in the world is most worthy of preservation. On an international committee (our own British stock might not by any means necessarily qualify, but if by any chance it did) the sooner we encourage a positive attitude towards the increased production of healthy children to populate and justify the owning of our vast Commonwealth the better.

Sustained Utopian human conditions are an impossibility, either in Britain or elsewhere. Since the beginning of time (and long before F.P. was even thought of) war, disease, and famine have taken their toll of human life. Depressing though it may be to accept it, these scourges seem to be an inevitable feature of our existence on this planet. To pretend to assist in preventing them by measures such as your F.P. correspondents offer is to grossly over-simplify a vast and apparently insoluble problem.

—I am, etc.,

Berwick-on-Tweed. AGNES R. S. SADLER.

W.H.O. and Birth Control

SIR,—The organization of which I have the honour to be the president could not agree more strongly than it does with Dr. Ruth Dovey (June 21, p. 1354) that "the only hope is for the white people to perfect methods of birth control and to teach them to the more backward races before famine is upon us all." In view of the vast population in India and other Oriental countries, which has more than overtaken their food supply, the greatest urgency is for a simple method of birth control for Oriental use.

Whilst perfection is utopian, may I urge the use immediately of the best and most suitable method available for the poor masses in India, now tested for over 20 years, with a failure rate of only one in 2,000 after years of use—that is, the simple flat sponge and olive oil or other bland cooking oil? The sponge being too expensive for many Indians, they can substitute successfully the waste product of their own native spinning, making a pad of cotton waste which, dampened with their own cooking oil, gives immediate protection. Another value of this method is that it can be taught to women out of reach of clinical and medical help.

A pamphlet giving instructions is being sent free by our society to thousands in India at present in the hope that it may overtake the disaster for Indians involved in the teaching by Dr. Abraham Stone, of New York, of the so-called "safe period" or "rhythm method" under the auspices of W.H.O., the latter being a method entirely unsuitable for Indians and cruelly misleading to the people who use it.—I am, etc.,

Society and Clinic for Constructive Birth Control and Racial Progress. MARIE C. STOPES.

SIR,—I would like to protest strongly regarding the tone of Dr. David Pyke's letter (June 28, p. 1405). He adopts the materialist conception of world problems. He objects to any opposition to his family planning. More than that, he suggests totalitarian methods to get the Norwegian proposal put into force. He states: "The situation requires that we do more than acquiesce submissively in the embargo imposed by those whose religious sensitivities are offended." May I remind him of the teaching of the Catholic Church on this matter: (1) Birth prevention is wrong and sinful; (2) birth prevention is grievously wrong and grievously sinful; (3) the evil and the seriousness of the evil are intrinsic—i.e., in the act itself and not merely on account of its consequences; (4) birth prevention is therefore always grievously sinful and can never be otherwise; (5) all the foregoing apply to each individual contraceptive act.

Hence, when we say that birth prevention or the contraceptive act is intrinsically wrong, we mean that it is at variance with man's rational nature in such a way that each contraceptive act is a serious infraction of the essential relations of things as established by God and made known to us by our reason.

This is indeed "an affair of the greatest consequence," but not in the sense that Dr. David Pyke implies.—I am, etc.,

Birmingham. J. R. TIGHE.

SIR,—Dr. David Pyke's letter (June 28, p. 1405) is most interesting, but is not his solution of the population problem a bit faint-hearted? It appears that there are too many babies and too many old people, but Dr. Pyke only proposes to get rid of the former. Surely, in order to be logical and to avoid an intolerable burden on the age groups 15 to 65, he should also exterminate the elderly. There is a recent European precedent for this, and if any old man objects to being murdered Dr. Pyke can remind him of the bad form

of indulging in "religious sensitivities." Following this with legalized abortion, sterilization of the unfit, and judicious euthanasia, the population problem should be quickly solved. It will be altered, anyway, and then perhaps a reward will be offered to any young woman who will be so kind as to have a baby—once more following a recent European example.

Perhaps the United Kingdom delegate had some of this in mind when he suggested an adjournment.—I am, etc.,

Oxted, Surrey. E. L. STURDEE.

SIR,—The existence of W.H.O. is evidence of a general desire to attempt the resolution by reasonable and peaceful means of some of the global problems which are believed to be potential causes of war. In this sense W.H.O. is a religious enterprise which demands the approval and support of all truly religious men who reject the philosophy of Nietzsche. Dr. D. Pyke in his important letter (June 28, p. 1405) draws attention to the deep conflict in the minds of those who try to reconcile their loyalty to Roman Catholicism with the intentions of W.H.O. He has emphasized what is perfectly clear to anyone who examines these large issues with an open mind, the fact that W.H.O. is doomed to failure unless its activities include the restriction of population growth.

It is the duty of those in whom a conflict of values arises to attempt a sincere resolution of the conflict in their own minds, a process from which renunciation cannot be excluded. A willingness to attempt renunciation when this is inescapable is what distinguishes a sincerely religious mind from one in which persuasions have no more than an obsessional basis.

The rejection by Roman Catholics of certain methods of birth control apparently proceeds from a conviction that man is not entitled to use his knowledge to interfere with a natural sequence of events. Since epidemics, famine, and human diseases generally are usually natural occurrences, the taking of reasonable steps to avoid them should come under the same stigma as birth control. To be consistent, therefore, anyone who is opposed to the spreading of knowledge of methods of birth control on the grounds of illegitimate interference with nature should be opposed to many other proposals and activities of W.H.O.

W.H.O. is an organization inspired by the conviction that the reasonable application of scientific knowledge to human affairs will allow improved prospects of human welfare. Ignorance and religious prejudice are among the foremost obstacles met with in the conquest of disease. Those whose religious convictions require them to allow nature to take its course, as those who do not believe that science can solve human problems, should preserve their own integrity and that of W.H.O. by not lending their services to the organization.—I am, etc.,

London, N.13. HAROLD B. HEWITT.

T-piece Anaesthetic Technique

SIR,—May I now reply to the letters which followed my article "A T-piece Technique for General Inhalational Anaesthesia" (January 5, p. 28)?

First, I must thank Dr. Philip Ayre (February 9, p. 327) for his kind comments, which are greatly appreciated, coming as they do from the originator of the T-piece principle of inhalational anaesthesia. Need I assure Dr. Ayre that I personally do not consider his apparatus cumbersome?

I was surprised to read that Dr. F. F. Waddy (February 16, p. 384, and March 22, p. 654) considers a flow-rate of gases of 8 l./min. grossly extravagant, since this is only 1 l./min. in excess of the *minimum* flow rate advised (on good grounds) by Macintosh and Mushin (1946) for a semi-closed technique—e.g., Boyle's apparatus. If CO_2 accumulation is to be avoided, the flow-rate of fresh gases in a semi-closed (semi-open) technique must equal or exceed the patient's normal resting minute-respiratory-volume (M.R.V.). Macintosh and Mushin postulate a normal M.R.V. of 6 l., whereas Fulton (1940a) gives a figure of 8 l. I believe the latter figure to be more accurate, and have found an average M.R.V. of 7.5 l. during anaesthesia with semi-closed techniques. In the T-piece technique, the expiratory valve is replaced by a column of gases at atmospheric pressure.

In my article I mentioned two of the common causes of increased operative bleeding. These are accumulation of CO_2 and breathing against resistance. These two factors cause increased respiratory activity and increased peripheral (musculocutaneous) blood-flow, particularly in the thoraco-abdominal region (Wright, 1940; Fulton, 1940b), and increased venous pressure. Thus arteriolar, capillary, and venous bleeding are increased.

The various reasonable alternatives put forward by Dr. Waddy will not, in my experience, produce results in any way comparable to the T-piece technique for the above causes, which must inevitably follow the techniques he mentions. First, a semi-closed (semi-open) technique depends for its operation on a positive pressure in the apparatus during expiration, the pressure required to inflate the rebreathing bag being 10–40 mm. water; in addition, a minimum pressure of 20–40 mm. water is required to "blow-off" most expiratory valves; finally the flow-rate suggested by Dr. Waddy (5 l./min.) will lead to about 40% rebreathing, or inhalation of a CO_2 concentration around 1–2%, with obvious consequences. His next suggestion of a lower flow-rate with CO_2 absorption suffers from the same disadvantages as regards the inflation of the bag and the expiratory valve, and in addition there is the resistance set up in breathing through the soda-lime, which I have found to be 10–30 mm. water with normal breathing. These figures are higher than those usually given, which are unaccountably low.

Now I would like to deal very briefly with the matter of cost. The alleged excessive cost of the T-piece technique amounts to a shilling or so per hour, or under two shillings for a case such as a mastectomy. In such a case, the "saving" on one item alone—namely, donated blood—is reckonable in pounds sterling. Bonica and Lyter (1951) state that the average blood-loss at mastectomy is 690 ml. and for this reason it is a common practice to give one or two bottles of blood to the patient. In my hands, using the T-piece technique, blood-loss averages 150 ml., and blood transfusion is seldom required. Thus a "saving" of perhaps £2 to £4 per case is possible on blood transfusion alone. Need I go any further in this matter?

Lastly, I am sure that nobody would recommend the T-piece technique as the method of choice in every case in a general hospital, so that I can see no point in basing any calculation on this assumption.—I am, etc.,

Southport JOHN BULLOUGH.

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Is Metallic Mercury Poisonous?

SIR,—In the interest of public safety I think I must protest against the views of Dr. D. H. Judson (June 28, p. 1406) that mercuric ions are responsible for the toxic effects of mercury compounds, which therefore vary in their toxicity according to the degree with which they ionize. One might thus be led to the belief that compounds like mercuric chloride and bromide, and, above all, dimethyl-mercury, are relatively non-toxic, since they ionize but little (in the last case not at all); in fact these are all highly dangerous substances.

One of the major factors influencing the toxicity of mercury compounds is *solubility* in either aqueous or lipoid media. Metallic mercury itself is fairly harmless, since it is insoluble in the various media present in the body and is not easily attacked chemically. The main danger from metallic mercury comes from its *vapour*, which would be responsible for numerous casualties—particularly in chemical laboratories—if it were not for the fortunate circumstance that all surfaces except when freshly formed are covered with a film of dirt (often invisible), which in the case of mercury greatly impedes vaporization. It is important to avoid exposure to constantly disturbed mercury surfaces or to mercury "powder"; in the last case the surface may be dirty, but the surface area is enormous.—I am, etc.,

Department of Physical and Inorganic Chemistry, University of Bristol. G. E. COATES.

SIR,—I had the following experience a few years ago: I was called to see a small boy aged 6 who had bitten through a clinical thermometer. The glass end was found, but not the mercury. I ordered stodgy food (suet pudding, bread, etc.), and a careful inspection of all stools. In due course the mercury appeared and the patient suffered no harm or discomfort.—I am, etc.,

Broadstairs, Kent. CASSIE E. B. WILLIAMS.

SIR,—An enterprising schoolfellow of mine used to drink large amounts of metallic mercury for bets. It did no harm whatever, except to those of us who had to pay up after the performance.—I am, etc.,

Portsmouth. J. A. U. MORGAN.

Tongue in the Nasopharynx

SIR,—A man aged 60 came to see me recently complaining of bilateral nasal obstruction which he said was due to a recurrence of his polypi, as "I can feel them with my tongue; they are on either side of a ridge at the back of my nose." I presumed that he was referring to the posterior free margin of the nasal septum and the backward extensions of the polypi. I could not help wondering at this seeming reduction of normal pharyngeal sensitivity, so I asked him to demonstrate his method. At once the tongue was dorsiflexed and rapidly introduced below the soft palate, and pushed well home into the nasopharynx (see illustration).

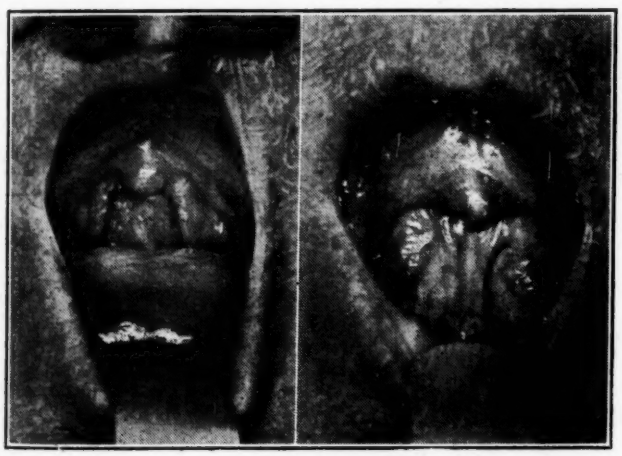


FIG. 1.—The tongue at rest: the soft palate appears normal.
FIG. 2.—"Lingual palpation." The uvula lies in contact with the frenulum.

He was able to hold this position quite comfortably for several minutes, and perform a systematic examination of the area, meanwhile breathing easily through the mouth.

The tongue itself appeared to be normal and the frenulum not unduly lax. Thus he was not able to touch the tip of his nose with his fully protruded tongue, a test suggested by Professor Victor Lambert. The soft palate itself, however, was rather high and flaccid and directed more anteriorly than usual.

The explanation I offer in this unusual case is based on his earlier history. He told me that when his polypi were first operated on in 1918 they were presenting below the palate. I presume that they so distorted the soft palate that the distance his tongue had to move was reduced. He told me that he had been practising this performance of lingual contortion from time to time since the end of the first world war.

I wish to thank Dr. Robert Ollerenshaw for his help in this case and Mr. R. Schofield, who took the photographs for me. A cinematograph film recording was also made. I also wish to thank Professor Victor Lambert for the interest he has shown in this amusing clinical diversion.

Since this case, I have examined a hospital resident medical officer who can perform the same feat with his tongue. This must indeed be an unusual coincidence. He can easily reach right round the tip of the nose to the middle of the dorsum with his tongue. The nose and post-nasal space are quite clear on ordinary clinical examination.—I am, etc.,

Manchester. NORMAN APPLETON.

College of General Practice

SIR,—In the *Supplement* to your issue of June 28 (p. 335) you publish a long article on "A College of General Practice" by Dr. John Hunt. In this, he quotes a long paragraph from my address "The Birth of a College" summarizing the opposition we met in founding the Royal College of Obstetricians and Gynaecologists, the weakness of the College at birth, and its wonderful development in the neonatal period. All this is true, but Dr. Hunt apparently has not appreciated the cause of this remarkable growth.

The objects for which the Royal College of Obstetricians and Gynaecologists was founded may be summarized as:

(1) To establish a portal through which must pass all those who desire to practise as consultants in this subject, a portal to consist of compulsory training in recognized hospitals and a stiff test of knowledge acquired in that time.

(2) To band together those practising this branch of medicine so that they can demand adequate facilities for teaching and training.

(3) To prevent the divorce of obstetrics and gynaecology.

This College has never asked for facilities to improve the material lot of its Fellows and Members.

Its rapid growth is due to the fact that the profession and the lay public quickly realized that its only objects were the improvement in the training, teaching, and practice of obstetrics and gynaecology, and that its membership is a guarantee of basic training and the passing of a stiff examination. Now, less than a quarter of a century after its foundation, it is rare indeed for a man to be appointed a consultant in this branch who is not a member of this College.

Have Dr. Hunt and his associates the same target in view—a comparatively small body of highly trained and examined members, a group of super general practitioners? There is nothing in the tentative and somewhat nebulous suggestions on p. 337 to suggest this, nor does it seem likely that such a small select body would do what the promoters seem to desire—namely, to raise the standard of practice throughout the whole body of general practitioners. Certainly such a select body would meet with great opposition from the large body of practitioners who were not qualified to be admitted. What seems to be the object of the promoters is the foundation of some large body which all practitioners may aspire to join, provided their work and ethical conduct generally commend themselves. Such a body would have great power for good, but it is not a "College." Rather does the word "association" seem suitable, such as both the physicians and surgeons designate the bodies whose membership is not limited to Fellows and Members of the Royal Colleges.—I am, etc.,

Manchester. WM. FLETCHER SHAW.

SIR,—A College of General Practice may or may not be a good thing from an academic point of view. I am certain, however, that it will not in itself raise the status of general practitioners one jot in the eyes of consultants, the public, or each other. Consultants will continue to judge general practitioners by the cases which are sent to them and by the quality of the accompanying case histories. The public will continue to judge the doctor by the manner in which he conducts himself and his examinations. Most important of all, the general practitioner will judge himself by the values he has set on his work.

I feel that there are few practitioners to-day who feel the same pride in being known as "the doctor," as they did before the advent of the National Health Service. The truth of the matter is that we are no longer our own masters. We have meekly accepted the public and the State as our masters, with only the occasional (polite) grumble—to each other. When the recent award was announced there were yelps of glee all round for the crumbs brushed to us. I do not really believe that the delight expressed was entirely due to the fact that a practitioner's skill would in future be assessed at 17s. for the care of one person for one year. Rather I feel that much of the jubilation was in response to the feeling that at last we had stood our ground, hit back, and won a round.

There is a disease abroad in general practice. Tonics, such as the award, or a new suit of clothes, in the form of a College of General Practice, help for just a while. But these are symptomatic measures, not specific treatment.

It is very much the case of "Physician, heal thyself." You do not need a psychiatrist to tell you why you experience this feeling of malaise or why others have lost their respect for you.

If we have a College of General Practice let us not make the mistake of looking to it to solve all our problems and take all our responsibilities, as so many others look to the State to-day. Nor let it detract our attention from the fundamental cause of the decline of general practice. Service to the public or State is one thing, servility another.—I am, etc.,

London, N.22. D. SILVER.

SIR,—Many of us will have been greatly heartened by the remarks concerning a College of General Practice (June 28, p. 1410). Dr. J. H. Hunt has appealed for funds to help this project. May I suggest that all who are interested contribute 2% of our back-money payment which we are to receive from the Danckwerts award? Half could be sent within the next three months and the remainder when we get the money from the Ministry.

May I suggest another duty of the college? We are continually bombarded with advertisements from the drug firms about new products. The value of these products seems to vary inversely with the amount of advertising the firm indulges in. Could not the proposed college let us have some medical evidence on the value of such new products? In America there is such a body which publishes its findings in the *J. Amer. med. Ass.* I am sure that official and expert advice on a drug's efficacy would greatly help to reduce unnecessary prescribing of proprietary preparations—especially in view of the modern craze for products compounded of more than one standard drug.

In conclusion may I ask the Steering Committee of the new college not to forget doctors in small towns far from big teaching hospitals.—I am, etc.,

Lincoln. A. H. FERGUSON.

Sport and Medicine

SIR,—A British Association of Medicine and Sport has recently been formed. Its aims are to promote the study and investigation of the medical and scientific aspects of sport in all its branches. Membership will be open to medical representatives nominated by all national sporting bodies and to any interested medical men and women with a qualification registrable in the United Kingdom. It is hoped that this association will attract a large membership of doctors. Those who are interested are invited to write for particulars to the Hon. Secretary, British Association of Medicine and Sport, c/o British Olympic Association, 71, St. George's Square, London, S.W.1.—We are, etc.,

London, W.1. ADOLPHE ABRAHAMS, President.
ARTHUR PORRITT, Chairman.

POINTS FROM LETTERS

Lipoma of the Hypopharynx

Dr. A. D. Morgan (London, S.W.1) writes: Dr. J. B. Penfold's report (June 14, p. 1286) of a large pedunculated lipoma of the hypopharynx causing death by asphyxia is reminiscent of a similar tumour reported by Mr. Holt on March 7, 1854 (*Trans. Path. Soc.*, **5**, 123), with a colour plate. The specimen is preserved in the museum at Westminster Medical School. The patient had symptoms for 12 years. Microscopically the tumour was a typical lipoma. A similar but much smaller (symptomless) tumour was encountered during a recent necropsy at this hospital.

Succinic Acid in Reiter's Disease

Dr. R. VARA LÓPEZ (Burgos, Spain) writes: Reiter's syndrome, characterized by a conjunctivitis, urethritis, and polyarthritis, since very seldom only one articulation is affected, sometimes accompanied by other symptoms such as diarrhoea and cutaneo-mucosal affections, in spite of being uncontrolled by a number of treatments has been treated successfully with A.C.T.H. and cortisone. Following the indications of my colleague Professor Rodriguez Candela, and the cortisone-like properties observed by him of succinic acid, we employed this product in 2% solution on a patient 44 years old, who in 1935 suffered a Reiter's syndrome which lasted four months and recurred in 1950, the symptoms lasting from December till May, though not diagnosed on either occasion as Reiter's syndrome. In February, 1951, urethritis, conjunctivitis, polyarthritis, balanoposthitis, and febricula reappeared. The administration of four phials of 0.15 g. and four of 0.30 g. of "neosalvarsan" did not modify the clinical picture; on the other hand, the intravenous injection of 10 ml. of 2% solution of succinic acid daily cleared the conjunctivitis on the third day of the treatment, the urethritis on the sixth day, and the polyarthritis on the fifteenth day. After 15 months the cure persists.

Incubation of Chicken-pox

Dr. LINA POTTER (London, N.1) writes: When I was a medical student there was a case of chicken-pox in the hostel where I was living. My mother was morbidly afraid of infection for my sister. I was planning to visit her at the end of three weeks, when someone told me that the incubation period might be 23 days—so I allowed 28 days to elapse. In the final week in which I had *not* visited home my sister developed chicken-pox. It is difficult to eliminate the long arm of coincidence in some of the commoner infections.

Geography of Hunger

Dr. O. D. GILMORE (Highworth, Wilts) writes: It is distressing to read in the correspondence columns of the *Journal* such letters as those of Drs. David Pyke and Ruth Dovey advocating the immoral practice of contraception as the cure-all for world problems. The pessimistic proclamations of Malthus have been proved by posterity to have been completely unfounded, as the nauseating nostrums proposed by the Neo-Malthusians are now confounded by the evidence put forward by de Castro in *Geography of Hunger*, which in the words of that great scientist, Lord Boyd Orr, "gives well authenticated facts to show that there is no physical difficulty in doubling or redoubling the world food supply. If the farmers fail us, the chemist has already shown the way to synthetic food . . . a world food plan . . . the only means of fulfilling the promise of freedom from want, though welcomed by most governments, was rejected by the U.S.A., the U.K., and the U.S.S.R. . , . The story of the economic domination of the earth, and the exploitation of the people and natural resources of weak nations by Western European nations in the last three hundred years and since the Spanish American War by the United States, here set forth fully documented, is a shock to anyone with preconceived ideas of the glories and virtues of our western civilization. It is a story of a ruthless fight for wealth with little regard for the rights or welfare of 'inferior races.'" This indictment of the "white people" to whom a correspondent so smugly wishes to "teach" immoral practices abhorrent to the majority of the "backward races" calls for an immediate and searching examination of our individual consciences, for we are responsible for this truly horrifying state of affairs in that we have not urged our Government to implement standard 5 of the Atlantic Charter or standard 5 of the Ten Points of 1940 of the Archbishop of Canterbury and his fellow Christians.

Correction

Dr. CHARLES CUGEL (Sydney, Australia) writes: Sándor Korányi was not a specialist on traumatic diseases (as stated in the *Hungarian News and Information Service* announcement, May 3, p. 951. He is the founder of modern kidney pathology. He was the first who introduced the determination of the freezing point of the blood into the clinic.

Obituary

SIR PERCIVAL HORTON-SMITH-HARTLEY, C.V.O., M.D., F.R.C.P.

Sir Percival Horton-Smith-Hartley, who died on June 30 at the age of 84, had a distinguished career as a physician. He was on the staff of St. Bartholomew's Hospital and the Brompton Hospital for many years. Percival Horton-Smith was the eldest son of the late R. H. Horton-Smith, K.C. He assumed the additional surname of Hartley in 1904, in accordance with the will of his father-in-law, the late Lieutenant-Colonel Joseph Hartley, whose daughter Josephine he married in 1895. From Marlborough College he went on to St. John's College, Cambridge, with a foundation scholarship. After taking a first class in both parts of the Natural Sciences Tripos he was later elected a Fellow of the College. He came up to Bart's with an entrance and a Shuter scholarship and graduated M.B., B.Ch. in 1893, becoming a Member of the Royal College of Physicians in the same year. Six years later he was elected to the Fellowship. In 1900 he gave the Goulstonian lectures on the typhoid bacillus and typhoid fever. He was for a time assistant physician to the Metropolitan Hospital, which was then largely staffed by Bart's men, who often were later appointed to the staff of their own hospital. It was in 1906 that he was elected to the staff of Bart's as an assistant physician. He retired under the age limit in 1932.

[Navana Vandyk Ltd., London

His chief interest lay in diseases of the chest, and he was appointed to the staff of the Brompton Hospital in 1899, where he did much valuable work. He was a Councillor of the Royal College of Physicians from 1918 to 1920, and an examiner for the Conjoint Board from 1926 to 1930. He also examined for Cambridge University and the National University of Ireland. In 1906 he was created M.V.O. and promoted C.V.O. six years later. He was knighted in 1921. Sir Percival was a member of the Worshipful Company of Ironmongers, and was Master of the Company in 1942–3.

Sir Percival Horton-Smith-Hartley's published work was chiefly concerned with diseases of the respiratory organs, but one of the most interesting articles he wrote was on the "Longevity of Oarsmen" (published in this *Journal* in 1939); it was based on the facts recorded in the *University Boat Race Official Centenary History*. In this paper he came to the conclusion that strenuous rowing, when combined with adequate training, did not lead to any diminution of longevity in healthy subjects. In 1931, in collaboration with Mr. H. R. Aldridge, he wrote a book on *Johannes de Mirfield of St. Bartholomew's, Smithfield*—a book replete with scholarship and learning.

Sir Percival was a type of physician all too rare nowadays. A classical scholar and a man of wide culture, he possessed a keen sense of humour and had a charming, though rather shy, personality. He was perhaps a little impatient when dealing with a large number of out-patients and did not suffer fools gladly, but he was kindness itself to patients in his wards. He was an indefatigable worker, not only in his hospitals but also in anti-tuberculosis work generally. He acted as joint secretary to the Advisory Committee set up to establish the King Edward VII Sanatorium at Midhurst. Up to three or four years ago he continued his active interest in all matters connected with tuberculosis until ill-health compelled him to give up all work. He is survived by his wife, a son, and a daughter, to whom we offer our sympathy.—C. M. H. H.

Sir Robert Young has kindly sent us the following appreciation: Sir Percival Horton-Smith-Hartley was a cultured physician, a very able clinician, and a loyal and friendly colleague. He devoted himself specially to the study of diseases of the chest. He was elected assistant physician to the Brompton Hospital in 1899, physician in 1906, and consulting physician in 1926. After holding office as pathologist and curator of the museum from 1900 to 1904, he prepared a catalogue of the pathological specimens in the hospital museum. He was precise and cheerful in the study of the patients in the wards, and his rounds were well attended by students, who appreciated his teaching. Keenly interested in the Frimley Sanatorium from shortly after it was established, he helped in the preparation of the statistical reports of the patients treated there. This work was published in 1924.

Sir Percival was joint secretary to the Advisory Committee appointed by His Majesty King Edward VII to establish the sanatorium at Midhurst, which bears his name. With the late Sir John Broadbent, his colleague as secretary, he visited, chiefly by bicycle, eleven sites before the selection of that at Midhurst. He helped in the award of the prize essay offered to medical specialists and architects to plan the lay-out of the building and its adaptation to the best interests of the patients, and he was present at the opening of the sanatorium by King Edward on June 13, 1906. One of the first physicians to the institution, he was afterwards on the council and on the medical committee.

His special interest in the problems of tuberculosis was evidenced by his appointment as a member of the council of the National Association for the Prevention of Tuberculosis, of which he was afterwards vice-chairman. He was an admirable member of the committees and was at his best as chairman, in which position his profound knowledge and great tact made him highly efficient. As an after-dinner speaker he was always successful. His style was witty, allusive, and admirably adapted to his subject, while his delivery was effortless and pleasing.

We are indebted to Dr. W. A. Bourne (Hove, Sussex) for the following appreciation: If one's chiefs must die, they should die old. Sir Percival Horton-Smith-Hartley was a good chief in this way as in others. But, as a result, even a generation ago he belonged to an older generation still, so that it was not immediately obvious to young physicians how he had earned the recognition he had received long before. He was splendidly equipped clinically, and the newer diagnostic methods were not as important to him as to the new diagnosticians. I remember his detection by percussion of what the radiologist called a small collection of fluid in the right costophrenic angle. When he heard the radiologist's opinion he smiled and said, "A *tour de force*," but whether his or the radiologist's was not clear. Looking back, it seems he must have passed beyond the stage where technical advances interested him as much as the great problems of disease as a whole—its prognosis and its dependence on environment, personality, and race. Thus, when I first read my notes of a case to him, he took me to the foot of the bed and whispered, "But tell me now, tell me now, you noticed—a Hebrew?" The problem of illness was one which he approached thus

from a broad viewpoint, so that he concerned himself in later years with general questions of expectation of survival rather than special concentration on individual cases. Among his house-physician's duties, however, were inspections of the "outlying parts of the ward"—kitchens, bathrooms, and lavatories—and regular tasting of the brandy provided for pneumonia cases. He carried a compass on his watch-chain, to decide whether a patient's room would get sun or not, and knew the dates of the Jewish festivals just as he did those of the Breton *pardons*. In making individual records he liked to use a quill pen with a big blue feather dipped ceremoniously into a special inkpot held for him by the ward sister, and this no doubt appealed to that humanist side of him which insisted on a long "o" when the word abdomen was read, and ordered cases to be treated *secundum artem*, and collaborated in writing *Johannes de Mirfield of St. Bartholomew's*. Such a combination of methods and viewpoints cannot have made teaching easy for him, yet he was most punctilious in hospital work: and to be under him was to be given a chance of learning from a physician of high intelligence and kindliness and conscientiousness, trained in the heyday of British clinical medicine. And more than that no one could have wanted.

The colleagues and friends of Dr. MARY NEVILLE ANDREWS heard with regret of her death in Lancaster on May 29 after a trying illness most cheerfully borne. She was a daughter of the manse and made an early acquaintance with general practice in her late 'teens after taking the diploma of the Apothecaries' Hall, for she acted as dispenser and book-keeper to a busy partnership in Bradford. After moving to London she attended the London School of Medicine for Women, and took the Conjoint diploma in 1916. After successive terms as obstetric assistant, casualty officer, and resident anaesthetist at the Royal Free Hospital she became medical officer in a large munition factory at Hayes, Middlesex, until the end of the first world war. In 1919 she graduated M.B., B.S., and in the following year she went to China as a medical missionary for the Methodist Missionary Society. She was responsible for a hospital in Pingkiang in the province of Hunan, but by 1925 China became so disturbed with rebellions, uprisings, and banditry that she had to flee the country, travelling by night and hiding by day for nearly a week, until she reached safety. Back in London she proceeded M.D. in 1926, and became research student and demonstrator in protozoology at the London School of Tropical Medicine, gaining her D.T.M.&H. in 1928. She again sailed for China to serve on the staff of the Henry Lester Institute in Shanghai, carrying out research in tropical diseases and parasites. She left this appointment about 1933, when conditions worsened as a result of the Japanese war in China, being evacuated by the British Navy. After a spell of inactivity from professional duties in London, yet still busy caring for others, she came north to Lancaster at the beginning of the recent war, and was soon busily engaged in general practice in Lancaster and district, as well as acting as honorary anaesthetist at the Royal Lancaster Infirmary. About four years ago an increasing dyspnoea compelled her to retire from active practice, though she was still able to enjoy her leisure in a limited way and to carry on as anaesthetist at the Infirmary. During the past year or so she was almost entirely confined to her room, between her bed and couch, but she maintained to the last that kindly interest in the welfare of others which gave a continuing outlet for those Christian principles that characterized her whole life. Patients thought and spoke well of her, for she gave them confidence when they were most anxious, by adopting a wise and friendly relationship which soon dispelled their fears. One could hardly credit from her unassuming nature that she had seen and done so much, yet her mind had acquired from wide experience, much reading, and varied travel a great store of knowledge. This, coupled with her ready sense of humour and richness of character, made her a very pleasant companion, with whom the hours passed quickly. She will be greatly missed.—R. G. H.

Medical Notes in Parliament

Raynaud's Disease

On June 30 Mr. J. T. PRICE asked whether the Minister of National Insurance would schedule Raynaud's disease within the terms of the Industrial Injuries Act.

Mr. O. PEAKE replied that the question whether this disease should be prescribed had been referred to the Industrial Injuries Advisory Council for consideration. He awaited a report. The cases were referred to the Industrial Diseases Subcommittee of the Advisory Council, which was in touch with the Medical Research Council on the medical questions which arose. The subcommittee would in due course receive the advice of the Medical Research Council. He himself was bound by the decision of the commissioners under the Industrial Injuries Act which decided that this disease did not fall within the terms of the Schedule.

Dysentery Increase

Mr. PATRICK MAITLAND on July 1 asked the Secretary of State for Scotland to account for a continuous rise in the number of cases of dysentery recorded in the 1951 report of the Department of Health, from a pre-war yearly average of 108 to 2,293 in 1949, 5,075 in 1950, and 6,004 in 1951.

Mr. J. STUART said that the 1951 provisional figure could be corrected to 5,302 as compared with an average of 1,142 in the five years 1935–9. The increase was largely due to better reporting of a mild type of the disease. The latest figure for deaths, 15 in 1951, compared favourably with the 1935–9 average of 30.

The Award

On July 2 Mr. JOHN ARBUTHNOT asked the Chancellor of the Exchequer to make a further statement arising out of the Danckwerts award.

Mr. R. A. BUTLER replied in writing that he wished to make it clear that the terms of reference of Mr. Justice Danckwerts's award were confined solely to the question of the remuneration of general practitioners in the National Health Service and that his award had no wider application. In accepting the results of the adjudication, which was of an exceptional nature, the Government had by no means adopted the view that similar adjustments in other fields should follow. In their view there was no justification for any assumption that the appropriate standard of remuneration for the professional classes was a rate of 100% above that in force in 1939. They considered that remuneration should be determined in the light of all relevant circumstances.

Diphtheria

Asked how many cases of diphtheria and deaths from that disease had been recorded in 1950 and 1951 in persons of 15 years of age and over, Mr. IAIN MACLEOD answered on June 30 that in 1950 there were 299 cases and 14 deaths; in 1951, 173 cases and 9 deaths. These figures related to England and Wales. In 1950 517,436 children were immunized, and 589,349 in 1951.

Prayers to Annul N.H.S. Charges

Several Prayers against regulations dealing with the National Health Service were jointly debated in the House of Commons on July 2, when Mr. HECTOR MCNEIL moved that the charges for dental treatment regulations dated May 23 be annulled. He hoped the Minister of Health would tell the House what he hoped to save by the deterrent effect of these regulations and what he hoped to gain by charges for prescriptions by doctors and hospital outpatient departments. From calculations by pharmacists in a town of some 90,000 people, Mr. McNeil found that in June, 1952, the number of prescriptions was down by just under 5% compared with June, 1951. He found that about 2% of the people who learned when presenting their prescriptions that there was a charge did not return for their

drugs. About 10% of them asked for receipts. Dr. B. STROSS said a definite hardship was discernible in the case of old-age pensioners, those suffering from acute chest complaints (including tuberculosis), diabetics, and people suffering from ulcer conditions. These had to pay 1s. or more practically every week. Mr. MCNEIL quoted a circular issued to hospital authorities (R.H.B. 52/56) which dealt with charges for prescriptions for hospital out-patients and said that hospitals should arrange that an officer was available when out-patient clinics were held to inform patients claiming exemption whether in fact they were exempt or not. The circular said that records should be kept of all exemptions and that the patient should be given a ticket or token at the dispensary to show that he was exempt. Mr. McNeil said this circular instituted a new type of snooper who had to sit with the sick and perhaps dying people in an out-patient department to see that the hospital authorities did not escape from the obligation of charging 1s. He believed that the professional staff would say their job was to cure and not to collect.

Mr. HUGH LINSTEAD said his information with regard to Scotland was that the average drop in prescriptions was about 15% comparing June this year with the average for the whole of last year, but the time was too early to draw substantial lessons from statistical returns. He agreed that the number of medicines made up but not called for was at present about 2%, which must be compared with the previous tendency under the National Health Insurance Act for about 0.5 to 1% of medicine not to be called for. In the terms of remuneration of chemists, the Minister had provided for a 1% non-collection. He noted that on the whole there had been a larger fall in consumption of medicine in the north than in the south.

Mr. SOMERVILLE HASTINGS said he had inquired at several hospitals about the impact of these charges on hospital services. He had learned that the people who raised most objection to the charges in the hospitals were the doctors and nurses. When a doctor had seen a colleague or nurse or perhaps another hospital worker and that person took the prescription to the dispensary and was asked to pay 1s. there was a strong feeling of resentment. Doctors agreed with the Scriptural injunction that it was wrong to muzzle the ox that treaded out the corn.

Mr. JOHN BAIRD said the regulations were creating so much trouble that already there was great deterioration in the dental health of the country.

Government Reply

Mr. IAIN MACLEOD, replying to points raised, said the amenity bed regulation (Statutory Instrument No. 1022) doubled the charges from 6s. to 12s. for single rooms and from 3s. to 6s. for small wards. It provided that, if the normal cost of treatment and maintenance was less than 24s. a day, the proposed charges should be proportionately reduced. There were just under 6,000 of these beds, 2,700 of them in mental, including mental deficiency, institutions. If all were occupied, the income would be about £400,000 a year, but a great number were required for patients who had urgent medical reasons for added privacy, and there had also been inadequate publicity given to these amenity beds. Consequently, the charges at present brought in rather less than half the possible amount. With the double charges, £800,000 should come in, but it might be the amount received would not be much more than half that. The experience of the Ministry was, however, that in England and Wales there was a considerable demand for such beds where their existence was known.

On the question of drugs and appliances dispensed at hospitals to the resident staff, Mr. Macleod said that if these patients were not treated in the ward they were regarded in the same way as the rest of the citizens and would normally be expected to pay the charge although there might be exceptions, because hospitals have their own methods of dealing with such matters. The biggest single problem was the question of ordinary drugs on a prescription percentage at a chemist's shop. There might be validity in the point that arrangements for persons on the border of extreme poverty or too proud to make use of the National Assistance service were not so clearly laid out as they should be. The poster issued by his department had made it clear that such people could, subject to a means test, obtain such remission. The propriety of assistance for authorized medicines or appliances was a matter for determination by the National Assistance Board. The arrangement for use in rural areas of postage stamps which were to be cancelled by the dispensing doctor or the chemist contractor had been worked out closely with the General Medical Services Committee. With regard to bottles of medicine dispensed by chemists but not collected, Mr. Macleod said an allowance was worked out that one prescription in 48 would be made to cover these contingencies.

Turning to dental treatment, he said that during the past month there had been a substantial fall in the demand for it and a substantial proportion of the estimates submitted had been for those who could claim exemption. The teeth of the priority classes would in future be better looked after than they had ever been. He then gave the position in relation to prescription charges. His general conclusion was that there had been something like a 15% drop in all, comparing June with June. It was impossible to give information on whether prescriptions were more costly than before. The National Assistance Board had made a spot check in two areas on appliances. In Leicester the number of applications from relief from the charges was four, and in St. Pancras none. For prescriptions there were ten applications, eight of whom were in receipt of assistance, and in St. Pancras ten applications, all of whom were in receipt of assistance. In Scotland from June 1 to June 24 the number of applications to the National Assistance Board on prescriptions by family doctors was 272 out of 1m. And out of that number 176 persons were already in receipt of National Assistance. The real question behind the debate was whether or not the regulations, and in particular the shilling on the prescription, would work. He contended that the regulations, and in particular the shilling on the prescription charge, implemented an undertaking given by Mr. Attlee and rested on the statutory authority of the 1949 Act of Mr. Bevan.

The Prayers for the annulment of the charges were then negatived.

Prescription Forms.—The estimated cost of the prescription forms brought into use since the 1s. charge was imposed is £4,862 in the present financial year.

Posters.—The cost of the posters stating that financial assistance is available in cases of hardship for charges under the National Health Service is estimated for England and Wales at £203.

Gold Teeth.—The value of gold supplied from official sources for essential dental requirements in 1951 was about £200,000 at the official price.

Universities and Colleges

UNIVERSITY OF LEEDS

Mr. F. P. Raper has been appointed Clinical Lecturer in Urology, from October 1.

UNIVERSITY OF SHEFFIELD

The following resignations have been received: Dr. A. G. Macgregor, lecturer in therapeutics, on appointment as senior lecturer in therapeutics in the University of Edinburgh, and Dr. Lorna H. Heslop, assistant medical officer in the Student Health Service.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

On June 6 Dr. J. F. Docherty was admitted to the Fellowship and Drs. Sarah L. Campbell and O. C. Ward were admitted to the Membership of the College.

FACULTY OF RADIOLOGISTS

The following candidates satisfied the Fellowship board at the June examination: *Radiotherapy:* S. Kramer, P. Strickland, H. C. Warrington. *Radiodiagnosis:* F. G. M. Ross, W. N. Thomson.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **June 21** (No. 25) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952					1951				
	Eng & Wales	Lond.	Scot.	N. Ire.	Eire	Eng & Wales	Lond.	Scot.	N. Ire	Eire
Diphtheria	23	2	2	0		37	5	10	1	1
Dysentery	145	34	77	90	3	567	105	103	3	
Encephalitis, acute	4	0	1	0		6	0	0	0	
Enteric fever:										
Typhoid	6	0	0	1		6	0	1	1	0
Paratyphoid	38	0	5 (B)	0	1 (B)	39	2	1 (B)	0	1
Food-poisoning	104	8		1		141	55		7	
Infective enteritis or diarrhoea under 2 years				19	30				15	40
Measles*	6,285	639	246	223	392	11,323	335	333	248	224
Meningococcal infection	33	3	17	0	1	28	4	19	0	1
Ophthalmia neonatorum	38	5	5	0		39	2	10	0	
Pneumonia†	383	24	158	2		396	13	185	1	2
Poliomyelitis, acute:										
Paralytic	49	6	7	5	1	44	1	6	4	1
Non-paralytic	19	1				35	2			
Puerperal fever§	269	40	17	2		85	2	8	1	
Scarlet fever	1,068	99	179	10	58	857	60	143	14	44
Tuberculosis:										
Respiratory			143	27				167	41	
Non-respiratory			27	5				22	2	
Whooping-cough	2,573	105	153	63	130	3,436	184	351	56	89

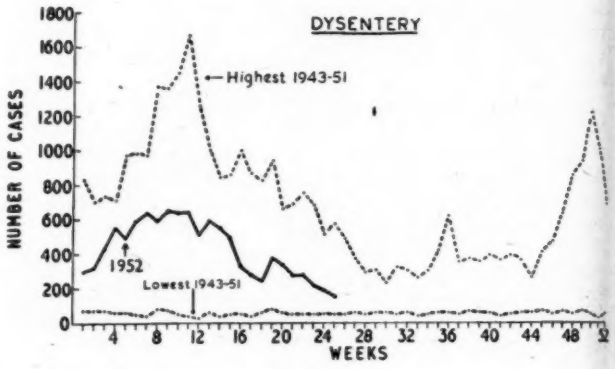
DEATHS in Great Towns	1952					1951				
	Eng & Wales	Lond.	Scot.	N. Ire.	Eire	Eng & Wales	Lond.	Scot.	N. Ire	Eire
Diphtheria	0	0		0	0	*1*	0	*0*	0	0
Dysentery	1	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	1	0		0						
Infective enteritis or diarrhoea under 2 years	3		2	3	3	*9*		*4*	1	1
Influenza	3	1		0	0	*2*	0	*0*	0	0
Measles		0		0	1		1	*0*	0	0
Meningococcal infection		0					0	*0*		
Pneumonia	135	28		6	2	*124*	15		9	10
Poliomyelitis, acute	1	0			0	*2*	0			0
Scarlet fever		0		0	0		0	*0*	0	0
Tuberculosis:										
Respiratory	114	16	17	2	8	*132*	27	6	6	12
Non-respiratory		4	4	0	1		0	*5*	3	2
Whooping-cough	1	0		0	1	*1*	0	*0*	0	0
Deaths 0–1 year	187	31	29	11	14	*243*	28	*35*	3	16
Deaths (excluding stillbirths)	4,235	604	483	104	176	*4,096*	645	*527*	102	128
LIVE BIRTHS	7,579	1203	913	234	440	*7,082*	1133	*909*	204	457
STILLBIRTHS	164	13	25			*195*	27	*32*		

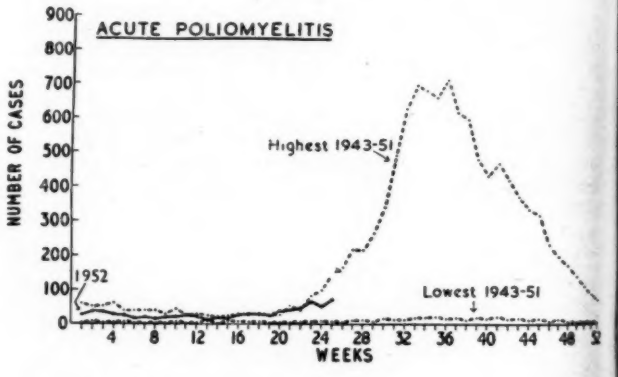
* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

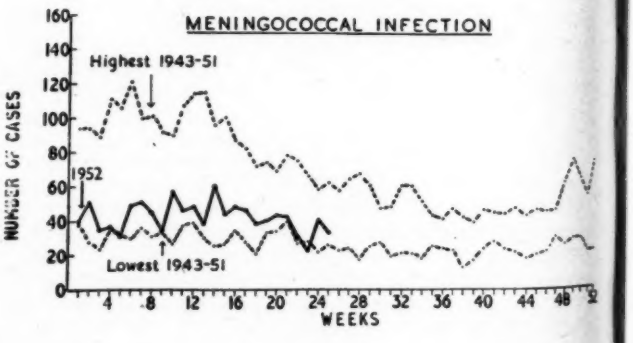
Vital Statistics

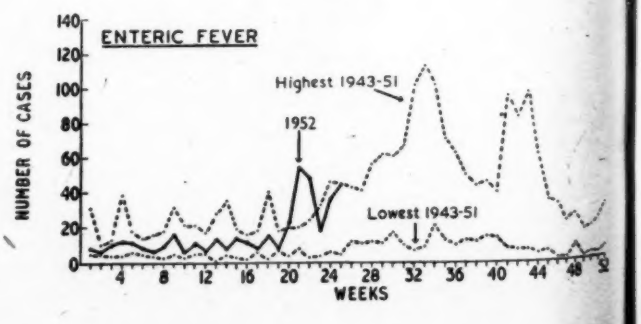
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1943–51 are shown thus -------, the figures for 1952 thus ———. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

Falls were recorded in the number of notifications of measles 1,022 and dysentery 43 in England and Wales during the week ending June 21, and rises were reported for scarlet fever 223 and whooping-cough 60.

Small rises in the incidence of scarlet fever occurred throughout the country. The largest was 40 in Lancashire. With the exception of a rise of 57 in Kent, there were only small variations in the local trends of whooping-cough. The number of notifications of diphtheria was 4 more than in the preceding week. The largest return was Birmingham C.B. 4. The largest decreases in the incidence of measles were Norfolk 192, Lancashire 166, and London 106.

The number of notifications of paratyphoid fever was 6 more than in the preceding week. This rise was due to the experience of Wales, where 17 more cases were notified than in the previous week. The chief centres of infection were Glamorganshire 23 (Cardiff C.B. 9) and Monmouthshire 5.

The number of notifications of acute poliomyelitis was 21 more for paralytic and 1 less for non-paralytic cases than in the preceding week. The largest returns were Durham 13 (Gateshead C.B. 6, Whickham U.D. 4, Felling U.D. 3), Yorkshire West Riding 9 (Leeds C.B. 3, Barnsley C.B. 2), and Warwickshire 4 (Birmingham C.B. 3).

The incidence of dysentery has declined for three consecutive weeks. The largest returns were London 34 (Wandsworth 10), Lancashire 18, and Southampton County 16. A further 90 cases were notified in the outbreak of dysentery in Antrim County.

Quarterly Return for Scotland

The birth rate during the first quarter of this year was 18.0 per 1,000 of the population, being 2 below the average of the five preceding first quarters. The infant mortality rate was 38 per 1,000 births and was 8 below the rate for the corresponding quarter of 1951. The stillbirth rate was 29 per 1,000 total births; this was the highest rate for any quarter of the past three years. The maternal mortality was the lowest ever recorded for any quarter, being 0.8 per 1,000 total births.

The general death rate was 14.5 per 1,000 of the population, and was 3.3 below the rate for the March quarter of 1951 and 1.0 less than the average rate for the five preceding first quarters. Two hundred and thirty-four deaths were attributed to the principal infectious diseases, 750 fewer than in the first quarter of 1951. They included 193 from influenza, 15 from whooping-cough, 14 from meningococcal infection, 8 from measles, and 4 from diphtheria. There were no deaths from typhoid fever or scarlet fever. The death rate for tuberculosis was 41 per 100,000 for respiratory and 47 for all forms; these rates were 22 and 26 respectively below the five-years average.

The number of marriages and the marriage rate were the largest for any first quarter since 1942.

Week Ending June 28

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,212, whooping-cough 2,444, diphtheria 33, measles 6,843, acute pneumonia 310, acute poliomyelitis 90, dysentery 135, paratyphoid fever 19, and typhoid fever 4.

Census Changes.—Population figures obtained at the 1951 census show that there are now 160 great towns (population over 50,000) in England and Wales instead of 126, and 17 principal towns (population over 30,000) in Scotland instead of 16. Therefore the 1952 figures for deaths, births, and stillbirths in these countries, published weekly in our Table, cannot be accurately compared with those for 1951, which are printed in italics. The 160 great towns in England and Wales have a population about 10% higher than the 126.

In the *Journal* of July 5 (p. 48) the upper half of the Table (showing cases) erroneously had two columns of figures printed in italics. They should have been in ordinary type.

Medical News

Is Chloramphenicol Dangerous?—A leading article in the *Journal of the American Medical Association*, June 28, p. 840, draws attention to the risks, hitherto largely overlooked, which treatment with chloramphenicol may involve. At least two types of adverse reaction are reported—a transient depression of the formed elements of the blood (red and white cells and platelets) during therapy, and a true aplastic anaemia which may be fatal. The latter complication may supervene in patients who have already completed one or two courses of chloramphenicol without incident. According to the *New York Times* of July 5 the U.S. Food and Drug Administration has set its entire staff on a nation-wide survey of patients receiving the antibiotic, and a spokesman has stated that over 200 new cases of aplastic anaemia had been observed in one week-end in those receiving the drug, while doctors had been advised for the time being to do blood counts on all patients receiving chloramphenicol as part of their treatment.

R.S.I. Prize Essay Competitions.—The council of the Royal Sanitary Institute has announced particulars of the prize essay open competitions for 1952. Three prizes are being offered: The Henry Saxon Snell Prize of 50 guineas for an essay on "The Selection, Utilization, and Hygienic Operation of Equipment for Cleansing Utensils, Crockery, etc., in Hotels, Restaurants, and Canteens." The John Edward Worth Prize of £40 for an essay on "The Design, Construction, and Fitting of Prefabricated Units for Cold and Hot Water Supplies and Waste Disposal in Housing Schemes." The John S. Owens Prize of £15 for an essay on "The Ventilation of Buildings used for Industrial Processes giving rise to Noxious or Unpleasant Dusts and Fumes, and the Prevention of Atmospheric Pollution by such Dusts and Fumes." Intending competitors should apply to the Institute, 90, Buckingham Palace Road, London, S.W.1, for a copy of the general conditions. Entries must be received by December 31, 1952.

Lister Institute.—The new director, in succession to Sir Alan N. Drury, F.R.S., who retires on September 30, is Dr. A. A. Miles, at present deputy director of the National Institute for Medical Research.

Dr. E. B. Chain, F.R.S., who worked with Sir Howard Florey on the isolation of penicillin at Oxford and is now guest professor of biochemistry at the Istituto Superiore di Sanità in Rome, was elected a *correspondant étranger* of the Académie de Médecine at its meeting in Paris on May 6.

NEW ISSUES

Archives of Diseases in Childhood.—The next issue of this journal (Vol. 27, No. 133) will be available in a week's time. The principal contents include:

MEGALOCYTIC DEFICIENCY ANAEMIA CURED BY SMALL AMOUNTS OF FRESH ENDIVE. C. M. H. Veeneklaas.

BLOOD FORMATION IN INFANCY: Part II. NORMAL ERYTHROPOIESIS. Douglas Gairdner, John Marks, and Janet D. Roscoe.

ACUTE IDIOPATHIC HAEMOLYTIC ANAEMIA. J. C. Millichap.

THE PATHOLOGY AND BIOCHEMISTRY OF GARGOYLISM. J. L. Henderson, Agnes R. Macgregor, S. J. Thannhauser, and R. Holden.

BRONCHOSCOPIC TREATMENT OF ATELECTASIS IN CHILDREN. B. Gans.

VARIATION IN THE PROTEOLYTIC ACTIVITY OF CHILDREN'S STOOLS: A STUDY OF MECONIUM AND STOOLS FROM NORMAL AND ILL CHILDREN. John L. Emery.

THE IMPORTANCE OF STAPHYLOCOCCI IN INFANTILE PARENTERAL GASTROENTERITIS. Paolo Tolentino.

METHYL TESTOSTERONE IN PREMATURE INFANTS. Ursula James and B. L. Coles.

THE INCIDENCE AND SIGNIFICANCE OF BREAST FEEDING IN INFANTS ADMITTED TO HOSPITAL. Patria Asher.

DENTAL CONDITIONS WITH ASSOCIATED SIGNS OF NUTRITIONAL DEFICIENCIES IN NEWFOUNDLAND CHILDREN. Helen Mellanby.

FUNCTION OF THE ADRENAL GLANDS IN THE NEWBORN. B. Wolman.
BILATERAL PHAEOCHROMOCYTOMA IN A SIX-YEAR-OLD BOY. Catherine A. Neill and Gwen Smith.
SPONTANEOUS RUPTURE OF THE HEART IN THE NEWBORN INFANT. W. E. Hunt.
RUPTURE OF A MYCOTIC ANEURYSM OF THE THORACIC AORTA. S. N. Javett and E. Kahn.

Issued six times a year; annual subscription £3 3s., single copy 12s. 6d.

British Journal of Ophthalmology.—The next issue of this journal (Vol. 36, No. 7) will be available in a week's time. The principal contents include:

LAMELLAR CORNEAL GRAFTS. CLINICAL REPORT ON 62 CASES. B. W. Rycroft and G. J. Romanes.
POLYMYXIN E. PENETRATION INTO THE EYE AND THERAPEUTIC VALUE IN EXPERIMENTAL INFECTION DUE TO PS. PYOCYANEA. D. Ainslie and Charles Smith.
OPERATIVE TREATMENT OF CONGENITAL PTOSIS. A REPORT ON 25 OPERATIONS. G. I. Scott.
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British Journal of Venereal Diseases.—The next issue of this journal (Vol. 28, No. 2) is now available. The principal contents include:

PATHOGENESIS OF THE JARISCH-HERXHEIMER REACTION. Albert Heyman, Walter H. Sheldon, and Lilian D. Evans.
VISCERAL ANALGESIA. A. S. Grimble and G. W. Csonka.
TREPONEMAL IMMOBILIZATION TEST. Pierre Durel, André Sausse, and Louis-Jacques Borel.
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THE PLEUROPNEUMONIA GROUP OF ORGANISMS AND THEIR SIGNIFICANCE IN GENITAL INFECTION. D. G. ff. Edward.
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COMING EVENTS

Medical Society for the Study of Venereal Diseases.—The Society's general meeting will be held in London, at 11, Chandos Street, W.1, on July 25, at 7.30 p.m. Dr. R. A. Nelson will read a paper on the serological diagnosis of syphilis. On July 26 the annual general meeting will be held at 11 a.m. at St. Mary's Hospital, Paddington. Details of the meetings and the informal dinner on July 26 may be obtained from Dr. W. N. Mascall, 39, Devonshire Place, W.1.

Institute of Medical Laboratory Technology.—The triennial conference will be held in London from July 28 to August 1 at the London School of Hygiene and Tropical Medicine. A trade show has been arranged for Wednesday, July 30, and anyone responsible for the purchase of laboratory equipment will be welcome. Full details of the programme may be obtained from the conference secretary, L. A. Willis, 34, Queensdale Road, W.11.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, July 14

INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Great Ormond Street, London, W.C.—5 p.m., *"Some Aspects of Paediatric Endocrinology,"* by Professor L. Dods (Sydney).

Tuesday, July 15

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—5 p.m., *"The Dangers of Chronic Inactivity in Old Age,"* F. E. Williams Lecture by Mrs. Margaret Hill.
SOCIETY FOR THE STUDY OF ADDICTION.—At Courtauld Lecture Theatre, Middlesex Hospital, Mortimer Street, London, W., 5 p.m., *"Recent Swedish Investigations on the Effect of Small and Moderate Doses of Alcohol on Driving Performance and Road Safety,"* by Professor L. Goldberg (Stockholm). A discussion will follow.

Wednesday, July 16

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—5.30 p.m., *"The Frequency of Ear Diseases and the Prevention of Deafness,"* by Professor Urpo Siirala. (Turku University, Finland).

Thursday, July 17

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At 26, Portland Place, London, W., 7.30 p.m., Symposium: *"New Antimalaria Drug—Daraprim,"* by Brigadier J. S. K. Boyd, F.R.S. Speakers will include Dr. G. H. Hitchings, Mr. I. M. Rollo, and Dr. L. G. Goodwin.

Friday, July 18

CAMBRIDGE UNIVERSITY.—At Department of Pathology, 5 p.m., *"An Experimental Inquiry into the Criteria of Neoplastic Change,"* by Dr. Peyton Rous (New York).
ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—5 p.m., *"Sir John Tomes—a Great Dental Pioneer,"* Charles Tomes Lecture by Mr. V. Zachary Cope.

APPOINTMENTS

FOWLER, A. W., M.B., B.S., F.R.C.S., Orthopaedic Registrar, Winford Orthopaedic Hospital, Bristol, South-western Regional Hospital Board.
REES-JONES, THOMAS GLYN, M.R.C.S., L.R.C.P., House-surgeon, Royal Berkshire Hospital, Reading.
SIMM, FRANCIS, M.R.C.S., L.R.C.P., Assistant Medical Officer of Health, Warrington, Lancashire.
SUMMERS, H. A. H., M.B., B.Ch., D.P.H., Medical Officer of Health, Brixworth Rural District, Daventry Borough, Daventry Rural District, and Assistant County Medical Officer of Health, Northamptonshire County Council.
TAYLOR, ALEXANDER R., M.B., Ch.B., F.R.C.S.Ed., Consultant Neurosurgeon to Hospitals under Belfast Hospitals Management Committee.
WILSON, ROBERT, M.D., F.R.C.P.I., Member of Visiting Staff of Royal City of Dublin Hospital.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brown.—On June 16, 1952 at Bristol Maternity Hospital, to Enid, wife of Dr. N. J. Brown, of 171, Stoke Lane, Westbury-on-Trym, a son—Peter William.
Gluck.—On June 17, 1952, to Mary, wife of Bernard Gluck, F.R.C.S., of Cardiff, a second son—Daniel.
Mills.—On July 1, 1952, at the Maternity Hospital, Loveday Street, Birmingham, to Dr. Margaret Jane, wife of Wilfrid Mills, F.R.C.S., a son.
Pardoe.—On June 5, 1952, to Margaret, wife of Dr. J. L. Pardoe, of Church Cottage, Portishead, Bristol, a daughter.—Catherine Mary.
Phillips.—On June 25, 1952, at the Barratt Maternity Home, Northampton, to Fran, wife of John H. C. Phillips, F.R.C.S., a son.
Scott.—On July 1, 1952, to Esmé (formerly Pascall), wife of Dr. Leslie Scott, Trencrom, Southcourt Avenue, Bexhill-on-Sea, Sussex, a son.
Trent.—On June 27, 1952, at the London Clinic, to Muriel (formerly Averbuch), wife of Dr. J. L. Trent, of 7, Hylda Court, St. Albans Road, London, N.W., a sister for Pamela Susan—Helen Elizabeth.

MARRIAGES

Pirrie—Hamilton.—On July 1, 1952, at Glasgow, Robert Pirrie, M.B., Ch.B., to May Hamilton, S.R.N.
Rey—Wood.—On June 21, 1952, in London, C. Humphrey J. Rey, M.R.C.S., to Thelma M. Wood.

DEATHS

Budden.—On July 4, 1952, at Laneside, Greywell, Hants, Charles William Budden, M.D., aged 74.
Currie.—On July 3, 1952, Patricia Quentry Currie, M.B., B.S., of Woodside, Burdon Lane, Cheam, Surrey.
David.—On July 5, 1952, at his home, Fyfield, Ongar, Essex, Archibald Sinclair David, M.R.C.S., L.R.C.P., D.P.H.
Hare.—On July 2, 1952, at his home, 83, York Road, Birkdale, Lancs, Alfred William Hare, M.B., Ch.B.
Hunter.—On July 1, 1952, at Highfield, Falkirk, Andrew Edwin Hunter, M.D.
Macleod.—On July 3, 1952, at St. Thomas' Hospital, London, S.E., Henrietta Mary Macleod, M.B., B.S.
MacLeod.—On June 22, 1952, at a London hospital, Neil Ferguson MacLeod, M.B., Ch.B., of 61, Uxbridge Road, London, W., aged 34.
Read.—On July 3, 1952, Charles Read, L.R.C.P.&S.Ed., F.R.F.P.S., L.D.S., F.D.S.Ed., of Albany Mansions, Renfrew Street, Glasgow, C.
Schaffter.—On June 27, 1952, Charles Merill Schaffter, O.B.E., M.B., F.R.C.S.Ed., of St. Andrews House, Matlock, Derby, late of Persia.
Stallard.—On June 27, 1952, at a nursing-home, Hindhead, Surrey, Hamilton George Frampton Stallard, L.R.C.P.&S.Ed., L.R.F.P.S., Lieutenant-Colonel, R.A.M.C., retired, of Redhearn, Churt, Surrey, aged 80.
Stanford.—On June 22, 1952, at a London hospital, Brigid Stanford (formerly O'Beirn), M.B., B.Ch., of 86, Glover Road, Scunthorpe, Lincs.
Young.—On June 30, 1952, at Oakwood, Bridge of Allan, Stirlingshire, Robert Tannahill Young, M.B. Ch.B., D.P.H.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Holiday Precautions for Thirsty Babies

Q.—*We are going to a remote part of France for our holidays. For how long must milk and water be boiled to make them safe for an infant?*

A.—The risk anticipated is presumably from the presence of organisms of the enteric group. These, and indeed all other bacteria causing milk-borne infection, including the tubercle bacillus, are much more readily destroyed by heat than is generally supposed, or than this question implies. Pasteurization can be depended on to destroy them, and this consists in maintaining a temperature of about 63° C. for 30 minutes (holder process) or 72° C. for 15 seconds (high temperature short time or flash process). It is therefore unnecessary to raise the temperature to boiling point, still less to boil for any specified period of time. To be on the safe side, and to obviate the necessity for using a thermometer, it is a satisfactory rule simply to bring milk to the boil.

Pressure Cookers and Infants' Feeds

Q.—*Are there any special advantages in using a pressure cooker to sterilize infants' feeds?*

A.—The use of a pressure cooker has been advocated for in-bottle sterilization of infants' feeds because it can ensure absolute sterility of the milk—i.e., the destruction of all bacteria, including heat-resistant sporogenous types: these are non-pathogenic, but may cause souring or putrefaction in milk kept for some time. It is thus possible to prepare a whole day's feeds at one time, regardless of the temperature at which they are to remain until all have been used. It has no special advantages as a safeguard against infection, since lower temperatures properly applied have the same effect.

Loss of Libido in the Male

Q.—*What treatment is advised for a healthy man complaining of decreased potency and libido? Is hormone therapy worth while, and, if so, what form should it take?*

A.—The answer to this question depends on the diagnosis. If we can accept the wording as meaning that the patient has no organic disease and no endocrine deficiency, then hormone therapy has no value whatsoever; in fact testosterone therapy is appropriate only when the testicle is secreting little or no testosterone, and it is then extremely efficacious.

In general, most cases of decreased potency and libido that come the way of the general practitioner or consultant are psychogenic, and psychotherapy is the appropriate treatment. If the case is severe, psychotherapy is often without benefit; if the case is moderate psychotherapy is helpful. In many cases the condition will respond to the good advice of an intelligent doctor, taking into account the whole background of the patient. It is perhaps not generally realized, but in the writer's experience it is true, that phases of decreased potency and libido can be considered as normal and attributable to the stress and strain inherent in modern civilization. Reassurance and patience will effect much in such cases. In diabetes mellitus, impotence is not extremely uncommon but is rarely associated with diminished androgen secretion. It may be psychogenic, or it may be associated with changes in the blood vessels or nerves concerned with penile erection. In any case it rarely responds to testosterone.

Permanent Waving Solutions

Q.—*What toxic or other hazards are associated with the use of permanent waving solutions? I have heard complaints of loss of hair and premature greying following their application.*

A.—The risks to hairdressers using permanent waving solutions of which thioglycolic acid is a constituent were mentioned in "Any Questions?" (December 22, 1951, p. 1534) under the heading "Coiffeur de Dames."

It is presumed that the present inquiry refers to hazards to the person on whom permanent waving solutions are used at intervals of perhaps several months. These solutions may be applied by a trained operator, or in the form of "home perms" by persons with no particular experience in the use of cold wave solutions. Provided that instructions for use are strictly observed no damage to the hair or scalp will result. It is most important to rinse the hair thoroughly with the neutralizing solution. The thioglycolate acts by softening the keratin, allowing it to be "set" in waves or curls, and, if this action is prolonged because of failure to neutralize, the hair will break off. Changes in colour and loss of hair are particularly likely to occur in hair which has been treated with dyes or bleaching agents, and special care must therefore be exercised in using waving solutions on such hair.

Digestibility of Butter

Q.—*What constituent is absent or present in butter which makes it specially digestible? Like many others, I can digest butter but not ordinary fats.*

A.—No significant differences can be demonstrated in the digestibility and assimilability of butterfat and many other dietary fats in normal human subjects or experimental animals. The milk fat of the cow and other ruminants contains a relatively high content of short-chain fatty acids, but there is no evidence that these affect the digestibility or absorption of the longer chain fats. If any differences between the digestibility of butter and other dietary fats can be demonstrated in normal subjects it must be due to these short-chain fats or to non-fatty constituents. In abnormal subjects the characteristics of the dietary fat may be of more importance in absorption; thus fats containing large amounts of saturated long-chain fatty acids are not well absorbed in the sprue syndrome.

Prophylaxis of Haemolytic Disease

Q.—*Has any attempt been made to prevent haemolytic disease by giving the mother an exchange transfusion with antibody-free blood a few weeks before term, or when the antibody titre rises? Could the blood withdrawn be safely used for transfusion into Rh-negative patients who were not pregnant?*

A.—There are no published reports of attempts to prevent haemolytic disease by giving the mother an exchange transfusion. However, there is every reason to suppose that such attempts would be unsuccessful. In infants with haemolytic disease of the newborn the amount of free Rh antibody is often only halved following a relatively large exchange transfusion. This gives an indication of what might be expected in the mother; but in addition in her case the titre of antibody would almost certainly increase again to the pre-transfusion level, since the mother, unlike the infant, can form more antibody. To achieve any good effects it would presumably be necessary to diminish the amount of antibody in the mother's serum by a considerable amount and to keep the titre at a low level for many weeks. It might well be necessary to give daily exchange transfusions to achieve this, and the project does not appear to be feasible.

Blood withdrawn during such an exchange transfusion could be used for transfusion into Rh-negative patients who were not pregnant. However, if the person having the exchange transfusion had received many previous

transfusions she would be more likely to be a carrier of the virus of serum hepatitis, and this additional risk would have to be considered before using her blood for transfusion to other patients.

Anorexia Nervosa

Q.—*A girl of 15 with severe anorexia nervosa is being given electro-convulsive therapy, which results in only short-lived improvement. Has physical treatment now replaced the textbook insistence on isolation, vigorous persuasion, and skilled nursing in this condition?*

A.—The best treatment of anorexia nervosa still consists in removing the patient from all contact with home and friends and treating her with rest, encouragement, and controlled feeding in hospital. The results are usually excellent.

Fear of Pregnancy

Q.—*A patient of mine, after three years of marriage, has been unable to achieve intercourse owing to an intense fear of pregnancy. According to a distinguished psychologist she required a long course of re-educative treatment by a psychologist to correct these faulty ideas. This is economically impossible. I endeavoured to carry out this procedure and arranged for her to help in the wards at a local maternity hospital. This improved her outlook, and she was impressed by the happiness of young mothers and developed a desire for a child of her own. After a long period she witnessed a delivery, and at the conscious level was amazed at the ease with which the child was born and the satisfaction the mother experienced. A few days later, however, she became tense, distraught, and agitated, and her hopeful attitude towards an ultimate cure completely disappeared. What treatment can be recommended? Have the exponents of hypnotism any short cut to success? Might she have solved her difficulties if I had postponed her entrance to the labour ward for a longer period?*

A.—If specialist treatment by a psychiatrist is not available, sympathetic listening to the patient's complaint as she repeatedly tells it, meanwhile reassuring her that she may be able to work her way gradually to an understanding of how her trouble began and how it can be overcome, may help. If, when seen, she ceases to complain and does not know what to talk about, she can be asked to tell all she remembers or has heard about her own bowel and bladder training (especially whether she had periods of constipation treated by enemas or laxatives), intercourse, and childbirth. This may lead her to discover the source of her fear and the way in which it can be overcome. Her conscious worry about pregnancy certainly hides other fears which will have to be discussed before they can be alleviated.

With regard to hypnosis, it can of course be said that for centuries such treatment has helped some patients. One can also say that the help obtained by hypnosis depends more on the personality of the hypnotist and his relation to the patient than on the technique of hypnosis, but the type of patient who can be helped by hypnosis is not easy to select.

Most likely the hopefulness and hopelessness of such a patient will vary very much from time to time. Following any period when her hope increases (unless this hope leads to a radical change in her condition with success in intercourse), it will probably be followed by a period of depression and hopelessness. Even when she has improved sufficiently to have satisfactory intercourse, pregnancy would probably be associated with another period of depression and anxiety, from which in a shorter or longer time she might well recover. It is likely that both the satisfaction and hope she obtained while working in a labour ward and the later depression and hopelessness would have occurred in any case. In the long run, her new knowledge of how satisfactorily women can go through pregnancy and labour is unlikely to be other than a help to her.

Lucifers

Q.—*What is the chemical composition of the fumes from the burning head of (a) a "safety" and (b) a "non-safety" match?*

A.—The fumes are substantially the same in both "safety" and "non-safety" matches, though the proportion of the constituents—mostly sulphur dioxide, carbon dioxide, nitrogen, oxygen, and water—differs.

Case for Diagnosis

Q.—*The following case was seen recently: A soldier of 19 complained of pain over the right brow and face which appeared very severe; when left to himself he would sit holding his face. The pain was described as a dull ache. Examination showed hyperaesthesia limited to the ophthalmic and maxillary divisions of the trigeminal nerve. The corneal reflexes were brisk and equal. On the following day there supervened anaesthesia both to touch and pinprick over the areas previously hyperaesthetic. Corneal reflexes were preserved and normal. Palatal sensitivity was normal. There was no masseter or pterygoid weakness. Forty-eight hours later sensation had completely returned. What was the diagnosis?*

A.—Almost certainly the soldier's pain was genuine, probably due to a carious right upper molar or antral infection, and the trigeminal hyperaesthesia was the first reflex reaction. The succeeding anaesthesia was clearly functional, proved not only by its rapid complete disappearance but by the anaesthesia to pin and touch being limited to the superficial cutaneous area, and not involving the mucous membranes of palate, conjunctiva, and cornea. It is most unlikely for loss to pin and touch (thermal and pressure sensations in this case are not recorded) to be limited to two anatomical trigeminal divisions. In the pons and medullary nuclei tactile and pain trigeminal conduction are very dissimilar, the former being transmitted through the principal sensory nucleus in the upper pons, while the pain fibres run caudally in the descending spinal root, ending in its special medullary nucleus. These two sets of fibres then decussate quite separately and run up the opposite side of the pons rostrally in two separate bundles to the crus and thalamus.

NOTES AND COMMENTS

Stains and Medicinal Dyes.—Dr. T. A. HUNT (East Midlands Division, National Coal Board) writes: With reference to your question on stains and medicinal dyes ("Any Questions?" June 21, p. 1366), we find in practice in the Mines Surgeries in No. 5 Area of the East Midlands Division that gentian violet and brilliant green stains are removed from skin and materials by sal volatile or "instrument dettol." The instrument dettol appears to be more satisfactory and does not cause a soreness of the skin, as frequently occurs with sal volatile.

Correction.—In the article by Mr. A. H. Hunt on "The Surgical Treatment of Banti's Syndrome" (July 5, p. 4) an error occurred on p. 8, column 2, first paragraph under "Group IV: The Terminal Stages of Cirrhosis (Table IV)." The first sentence should read: "Table IV completes the background against which the results of this report must be judged."

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